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Anatomo-Radiological Correlation Comparing Anatomopathological Data from Radical Prostatectomy and Multiparametric Prostate MRI

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Abstract **Original Research Article**

Introduction: In order to characterize the clinical behavior of CaP, pMRI could, thanks to its ability to detect, localize and estimate tumor foci, distinguish silent from invasive and aggressive tumors. ***Materials and methods***: This is a retrospective study including 44 patients collected at the Urology Department of the Mohammed V Military Hospital in Rabat (HMMV) over a 22-month period, from January 2020 to October 2021. Mean age; PSAt; size, dimension and location of lesion on MRI; approach; histological type; positive surgical margins; extracapsular extension; perineural invasion; lymphovascular invasion; seminal vesicle invasion; lymph node involvement; PI-RADS and Gleason scores were collected. ***Results***: According to our study, the histopronostic factors corroborating with PI-RADS are: - Gleason score - extra-capsular extension - seminal vesicle invasion - lymphovascular invasion. ***Conclusion***: Multiparametric MRI offers convincing and promising results for the detection of suspicious lesions. Performed prior to radical prostatectomy, it provides essential information for diagnostic and therapeutic management.

Keywords: prostate cancer, radical prostatectomy, MRI.

INTRODUCTION

Prostate cancer is the most frequently diagnosed cancer in Morocco, after lung cancer [1]. Diagnosis is based on rectal examination, PSA measurement and ultrasound-guided biopsy. Despite the reliability of this approach, it has limitations that can lead to unwarranted invasive diagnosis and treatment. So, to characterize the clinical behavior of CaP, from silent to invasive and aggressive tumors, other diagnostic means can be employed for better management. Multiparametric magnetic resonance imaging (mpMRI) could meet this need, with its ability to detect the most aggressive cancers. The American College of Radiology (ACR) has therefore developed a score, PIRADS, to help improve early diagnosis of clinically significant prostate cancer and reduce unnecessary biopsy and treatment of benign and sub-clinical tumors. Histopathological study of the prostate after radical prostatectomy has undeniable predictive value. We might therefore ask whether correlating anatomopathological data from radical prostatectomy with those from multiparametric prostate MRI would be a prognostic factor that would enable better stratification and management of CaP.

MATERIALS AND METHODS

This is a retrospective study including 44 patients collected in the urology department of the Hôpital Militaire d'Instruction Mohammed V de Rabat (HMIMV) over a 22-month period, from January 2020 to October 2021. The following data were collected: 1. clinical data: patient age, PSAt, PSAl 2. mpMRI data: prostate volume, lesion size, lesion side, lesion location, number of lesions. PIRADS score. 3. Approach. 4. Histopathological specimen data: Tumour volume, histological type, Gleason score, extracapsular extension according to side of extension, positive margins, Gleason grade at margins, peri-neural invasion, lympho-vascular invasion, seminal vesicle invasion, lymphatic invasion during lymph node dissection. 5. PI-RADS and Gleason scores. Inclusion criteria:- All patients who had mpMRI prior to radical prostatectomy. 3.2. Exclusion criteria:- All patients with radical prostatectomy without mpMRI.

- All patients with mpMRI but without PIRADS 3.3. Study population: Of 55 files, we selected 44 according to the above criteria. The search was carried out using the search database on the library of : - Pub Med - Science direct - Clinical Key Using the following keywords:- Prostate cancer - Prostate mpMRI - Radical prostatectomy - PIRADS score. Data entry and analysis were carried out using SPSS 23 for IOS (IBM corporation, ARMONK, NEW YORK, U.S.). Two types of analysis were chosen for the data analysis:- Uni-variate analysis: Categorical variables were described in terms of numbers and percentages, and the comparative study was carried out using Pearson's Chi-Square method of comparing percentages, or Fisher's Exact method (in cases where the expected number of participants was less than 5 in the Chi-Square method). A P <0.05 was considered statistically significant.

RESULTS

Exploitation of our archive over a 22-month period, from January 2020 to October 2021, allowed the exploitation of 44 radical prostatectomy files meeting the predefined inclusion criteria. The mean age of this population was 65.7 ± 6.31 with a maximum of 72 years. The mean PSAt was 10.1 ng/ml, with 59% of patients having a PSAt between 4-10 ng/ml. PSAt > 20 ng/ml was found in only 5% of patients. Analysis of mpMRI reports revealed a mean prostate volume of 44.6 ml +/- 7.6. Tumor size was between 2.1 and 3 mm in half (50%) of patients, and rarely > 3.1 mm (2%). PIRADS 3 was in the majority with 47.7%, followed by PIRADS 5 with 25%. PIRADS 2 and 4 were in the minority, with 6.8% and 20.45% respectively. Table 1 summarizes all our patients' clinico-radiological data. Laparoscopy was standard except in cases of contraindication or technical difficulty. Laparoscopy was performed in 2/3 of our patients (68%), divided between the transperitoneal route (45.4%) and the subperitoneal route (22.7%). Gleason 7 was the predominant score in 62.4% of patients. Followed by Gleason 6 in 21.1% of patients and Gleason 9 in 11.2%. Finally, Gleason 8 was in the minority, representing only 4.1% of patients. Extracapsular extension was found in 27.2% of patients, with no predominance of one side over the other, while positive margins were present in 34.5%. Tumor size greater than 1mm accounted for 62% of cases. Gleason grade at the margins is often unavailable. Pejorative factors, such as peri-neural invasion, are often present in 72.7% of patients. In contrast, lympho-vascular invasion is rarely found, in only 4.5% of cases. Invasion of the seminal vesicles was present in only 11.3% of cases, with no predominance of one side over the other. Lymph node dissection was performed in 56.8% of patients, with positive lymph node involvement in 4%. All these histological data are listed in Table 2. Univariate analysis showed that the post-operative Gleason score for PIRADS 3 and 5 lesions was statistically different, with a significant p-value ($p < 0.005$), as was that for PIRADS 4 and 5 lesions. There was also a significant correlation between PIRADS and other factors such as extracapsular extension, lymphovascular invasion and seminal vesicle invasion ($p<0.001$, 0.032, 0.007 respectively). However, this correlation was not found with age, surgical margins, peri-neural invasion and number of positive lymph nodes at lymph node curage. These data are summarized in Table 3. Nevertheless, multi-variate analysis of the correlation of PIRADS with these different histopathological factors, clearly shows a clear correlation of high PIRADS with high Gleason score, extra capsular extension and vesicular invasion. A summary of this correlation with histoprognostic factors is given in Table 4.

Table 1: Clinico-radiological characteristics of our cohort

Variables	N= 44
Middle age	65.7 ± 6.31
PSAt	10.1 ng/ml
PSAL	Non disponible
PSAt subgroup • 0-4 ng/ml • 4- 10 ng/ml • 10 – 20 ng/ml • > 20 ng/ml	n (%) 5 (11.4%) 26 (59 %) 11 (25%) 2 (4.5%)
Prostate volume	44.6 +/- 7.6
Lesion size • < 1 mm • 1.1-2 mm • 2.1 – 3 mm • > 3.1 mm	n (%) 7 (14.6%) 16 (33.3%) 24 (50%) 1 (2%)
Side of lesion on MRI: • Right • Left • Bilateral	n (%) 12 (35.3%) 16 (47%) 6 (17.6%)
Locating the lesion on MRI • Anterior • Posterior • Bilateral	n (%) 8 (43.7%) 9 (49.3%) 1 (7%)
Number of lesions on MRI • Double location • Single location	 14 (31.8%) 30 (68.18%)
PIRADS score • 2 • 3 • 4 • 5	 3 (6.8%) 21 (47.7%) 9 (20.45%) 11 (25%)

Table 2: Radical prostatectomy: approach and histopathological findings

Routes first: • Robotics • Open PR • Transperitoneal laparoscopic approach • Laparoscopic subperitoneal approach	 0 (0%) 14 (31.8%) 20 (45.4%) 10 (22.7%)
Average tumor volume (ml) Histological type, n (%) • Acinar adenocarcinoma • Ductal adenocarcinoma	Not available 43 (99.4%) 1 (0.6%)
Gleason score, n (%) • 6 • 7 • 8 • 9 • 10	10 (22.7%) 27 (61.4%) 2 (4.5%) 5 (11.4%) 0 (0%)
Positive margins n (%) • Apex • Anterior • Posterolateral • Bladder neck	15 (34.%) 3 (6.8%) 3 (6.3%) 5 (11.4%) 4 (9%)
Gleason grade at margins	Not available
Tumor size at positive margins, n (%) • Microscopic < 1 mm • Macroscopic > 1 mm	5 (38 %) 8 (62 %)
Extracapsular extension, n (%) Side of extra capsular extension • Right side • Left side • Bilateral	12 (27.2 %) 4 (33.3 %) 5 (41.6 %) 3 (25 %)
Peri-neural invasion n (%)	32 (72.7%)
Lympho-vascular invasion n (%)	2 (4.5 %)
Invasion of seminal vesicles n (%) Side of VS invasion n (%) • Right side • Left side • Bilateral	5 (11.3%) 1 (20%) 1 (20%) 3 (60%)
Lymphatic invasion - Lymph node dissection - Lymph node involvement n (%) - Side of lymph node involvement o Right o Left o Bilateral	 25 (56.8%) 4 (%) 1 (25%) 1 (25%) 2 (50%)

Table 3: Pathological findings according to PIRADS score.

Variable	PIRADS SCORE				
	2	3	4	5	P
Age	65 (64-69)	65.5 (57-74)	66 (50-76)	66 (53-86)	0.999
Gleason score • 6 • 7 • 8 • 9 • 10	 1 (33.4%) 2 (66.6%) - - -	 6 (28.5%) 15 (71.5%) - - -	 2 (22.2%) 5 (55.5%) 1 (11.1%) 1 (11.1%) -	 1 (9,09%) 5 (45.45%) 1 (9,09%) 4 (36.36%) -	 <0.001
Margins surgical	2.4%	14.6%	31.7%	51.2%	0.234
Extra capsular extension	0%	4.9%	26.8%	68.3%	<0.001

Variable	PIRADS SCORE				
	2	3	4	5	P
Perineural invasion	60%	65%	64.7%	79.2%	0.379
Lympho-vascular invasion	0	0	0	100%	0.032
Invasion of SV	0	0	15.4%	84.6%	0.007
Number of positive lymph nodes.	0	100 %	89.5%	81.5%	0.611

Table 4: PI-RADS correlation with histoprognostic factors

Variables		Estimation	SD	P	IC 95%	
					Lower limit	Upper limit
Prognostic factors	**Gleason score**	1.047	0.243	**<0.001**	0.821	1.179
	MCP +	0.648	0.363	0.074	0.359	1.244
	Extra capsular extension	1.933	0.410	**<0.001**	1.737	2.016
	SV invasion	2.436	0.801	**0.002**	2.121	2.735
	Number of positive nodes	0.999	0.352	0.066	0.690	1.123

DISCUSSION

Conventional diagnostic tools such as digital rectal examination (DRE), PSAt (Prostate Specific Antigen) and transrectal prostate ultrasound (TRUS) helped detect the disease, but with no distinction between significant and non-significant cancer. In fact, the consequence was over-diagnosis and over-treatment. In other words, cancers were diagnosed that should not have been detected, and others were operated on that should not have been treated. mpMRI has become an essential element in the management of prostate cancer, acting as a filter that detects significant cancer at risk of progression and requiring treatment. However, its role is still expanding, as it moves beyond the traditional diagnostic framework towards another, that of predicting histoprognostic factors. According to our study, the histopronostic factors corroborating with PI-RADS are : Gleason score, extra-capsular extension, invasion of seminal vesicles, lymphovascular invasion. The histopathological data obtained from the surgical specimen and used to stratify patients into groups at risk of recurrence and/or specific survival are the Gleason score, pathological stage and status of surgical excision margins. These criteria are widely validated in the literature, and are currently included in the tables of Partin *et al*., and the nomograms of Kattan *et al*., [2]. Assessing the status of the limits of resection is an important step. It is based on the presence or absence of tumour in contact with the indelible ink. This status is an independent prognostic factor, predictive of both local and systemic recurrence. However, the impact of positive surgical margins on specific survival remains formidable, depending on other prognostic factors and the initiation of adjuvant or salvage therapy [3]. Tumour volume at the margins and the number of positive sites are only poor prognostic elements and should be mentioned by uro-anatomopathologists. On the other hand, the location of the positive margin does not have an independent prognostic impact, but it remains a useful precision for urologists to promote their surgical technique. In our case, when analyzing the location of margins, we did not raise any particularities. It is legitimate to say that a poorly differentiated residual tumour is more likely to progress than a well-differentiated tumour, but this logical link has not been clearly demonstrated by studies and remains optional in prostatectomy specimen reports [4]. In our study, positive margins were seen in 15 patients, corresponding to a rate of 34.5%, which is in line with international centers (33.5%) [3]. In our cohort, 82.9% of positive margins were found in patients with PIRADS 4 and 5, while 17.1% of positive margins were found in patients with PIRADS 2 and 3. However, in univariate and multivariate analysis, no significant relationship was found between high PIRADS and the risk of positive margins. However, a prospective study including 154 patients has shown that PIRADS can help in decision-making regarding the extent of resection during radical prostatectomy without increasing the risk of positive surgical margins [5]. Involvement of the seminal vesicle is an important histoprognostic factor with a direct impact on the management of CaP. It enables us to distinguish localized from locally advanced cancer, and thus to assess the risk of recurrence. The study by Kwong Kim *et al*., on the prognostic value of seminal vesicle invasion on preoperative mpMRI, retrospectively analyzed data from 159 patients and found a direct relationship between seminal vesicle invasion and biochemical recurrence (p=0.049) [6]. A correlation between PI-RADS and seminal vesicle invasion is therefore relevant to our study. Analysis of our data shows a direct relationship between high PI-RADS and seminal vesicles invasion (p=0.007). The De Cobelli *et al*., study, which included 223 patients, found no relationship between PI-RADS and VS invasion (p=0.41) [7]. Another retrospective Korean study (Lim *et al*.,), published in 2021 in the Scandinavian Journal of Urology, included 569 patients and corroborated our study by finding a direct relationship between PI-RADS and seminal vesicles invasion (<0.001) [8]. The Gleason score is one of the most important histoprognostic factors. Adenocarcinomas form a broad spectrum of lesions, ranging from very well- differentiated to clinically significant, poorly differentiated cancers. The higher the Gleason score, the more severe the prognosis in terms of biological progression. The relationship between PI-RADS and Gleason score is therefore of

prime importance in demonstrating the relationship between mpMRI and pathology data. In our series, the Gleason 7 score was the most represented at 62.7%, and was evenly distributed across all PIRADS scores, apart from a non-significant increase for PIRADS 3. Gleason 6 is seen mainly (70%) in patients with a low PIRADS score of 2 or 3. However, Gleason scores 8 and 9 were seen exclusively in patients with a high PIRADS score 4 or 5. Univariate and multivariate analysis objective the correlation between a high PIRADS score and a high Gleason score and vice versa, with a significant p-value <0.001 (95% CI 0.821-1.179). The Sahin *et al*., study, which examined the relationship between mpMRI and histopathology prior to radical prostatectomy, retrospectively pooled data from 93 patients and found a significant relationship between PIRADS and Gleason score (P<0.001), in line with the results found in our study [9]. A multicenter American meta-analysis, involving 3349 patients and aimed at demonstrating the PPV of PI-RADS for the detection of high-grade prostate cancer, presented a result that was low and varied considerably from center to center [10]. This may be due to inter-reader variability among pathologists and radiologists, or to false negatives. The value of PI-RADS lies in its ability to distinguish clinically significant cancers. A retrospective study of 56 patients sought to demonstrate the role of PI-RADS2 in patients with Gleason 6 (3+3) biopsy. It demonstrated that PI-RADSv2 and the measurement of periprostatic fat using mpMRI can be correlated with pathological upgrading on the radical prostatectomy specimen and, consequently, accurately identify and monitor patients who are candidates for active surveillance [11]. Extracapsular extension of prostate cancer is a poor prognostic factor associated with progression, post-treatment recurrence and increased prostate cancer mortality. Accurate staging prior to radical prostatectomy is crucial in deciding whether or not to preserve neurovascular strips and possibly avoid positive margins. In our study, 12 patients, i.e. 27.2%, presented with a Extracapsular extension. This value is in line with that of other international studies (32.4%) [12]. We found that 95.1% of patients with Extracapsular extension had PI-RADS 4. Uni- and multivariate analysis of these data revealed a clear relationship between PEE and PI-RADS (p<0.001). This is in line with the retrospective study by De Cobelli *et al*., which included 223 patients and showed a correlation between PI-RADS and extra-capsular extension (p<0.001). Another prospective study involving 154 patients also corroborates ours, with a relationship between PI-RADS and Extracapsular extension (p < 0.05) [5]. Perineural invasion corresponds to isolated colonization of a nerve located in the periprostatic space, without invasion of the fat surrounding this nerve section [2]. It is predictive of lymphatic and vascular spread and can therefore be considered a poor prognostic factor. Perineural invasion is not one of the prognostic factors that PI- RADS can highlight in our study (p=0.379). This is in line with the prospective study of the impact of uni- or multifocal perineural invasion in prostate cancer during radical prostatectomy. It included 288 patients and found no correlation between PI-RADS and perineural invasion (p=0.258) [13]. It has been reported that lymphatic metastasis frequently indicates a poor prognosis and increases the postoperative probability of biochemical recurrence. To our knowledge, curage is the most direct and standard method for determining the presence of lymphatic metastases [14]. This raises the question of whether PI-RADS would enable a better assessment of lymphatic invasion. In our study, PI-RADS was associated with the risk of lymphovascular invasion (p=0.032), but only with the number of lymph nodes positive for curage (p=0.611). This contrasts with the Chinese study retrospectively pooling data from 316 patients with T2N0M0 and a Gleason score ≥ 3, which asserts that PI-RADSv2 was relevant in predicting the number of positive nodes (p<0.001) [14]. The limitations of our series are its retrospective nature, the small number of patients included in the study and the lack of centralized reading of the mpMRI, which presents a real problem in view of the inter-reader variability proven in the literature. However, some authors report that this bias has a minimal impact on the results [15]. The small sample size of this series led to the random absence of PIRADS 1 in our series.

CONCLUSIONS

Multiparametric MRI offers tangible and promising results for the detection of clinically significant suspicious lesions. Performed prior to radical prostatectomy, it provides essential contributions to diagnostic and therapeutic management. According to our study, the histopronostic factors corroborating with PI- RADS are: Gleason score, extra-capsular extension, invasion of seminal vesicles, lymphovascular invasion. Thus, the use of MRI as part of the prostate cancer diagnostic strategy is significantly favourable.

Conflicts of Interest : The authors declare no conflicts of interest.

Authors' Contributions: The authors participated equally. All authors read and approved the final version of the manuscript.

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