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Short Communication

Multiparametric magnetic resonance imaging/transrectal ultrasound fusion-guided prostate biopsy: a comparison with systematic transrectal ultrasound-guided prostate biopsy

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Background & Aims. Prostate biopsy is the standard method for diagnosing prostate cancer. Herein we compared the cancer detection rate of extended systematic Transrectal Prostate Biopsy with that of multiparametric Magnetic Resonance Imaging/Transrectal ultrasound fusion-guided Prostate Biopsy.
Methods. Outcomes of 99 fusion prostate biopsy (Group A) were compared with those of a matched population of patients having undergone systematic transrectal prostate biopsy (Group B) in the same period.
Results. The overall cancer detection rate was 60.6% in Group A and 29,2% in Group B (p = < 0,001) whereas the rate of clinically-significant prostate cancer was 26.2% in Group A and 13,1% in Group B (p = 0,02). At first prostate biopsy the above-mentioned rates were 76% in Group A and 31,9% in Group B (p < 0,001), whereas in repeated biopsy the rates were 34,7% in Group A and 18,6% in Group B (p = 0,08). Cancer detection rates correlated well with the Prostate Imaging-Reporting and Data System; in the setting of first biopsy, it was 84,6, 67,8, 100% for score 3, 4 and 5, respectively, whereas in the setting of repeat biopsy it was 28,5, 55,5 and 80% for score 3, 4 and 5, respectively. Complications rate was similar in both groups but all occurred in patients > 75y.
Conclusions. Multiparametric Magnetic Resonance Imaging/transrectal ultrasound fusion-guided biopsy provided better prostate cancer detection rates than standard Prostate Biopsy in the setting of both first and repeated Prostate Biopsy, showing good correlation between Prostate Imaging-Reporting and Data System scores and cancer detection rates but complications were more common in elderly patients.

Keywords: Prostate Cancer, Magnetic Resonance Imaging, fusion biopsy, systematic biopsy, detection rate

INTRODUCTION

Prostate cancer (PCa) represents the tumor with the highest incidence in Italy and its incidence significantly increase with age. Physicians however tend to be reluctant to recommend serum prostate-specific antigen (PSA) testing in men > 75 years as well as to advise prostate biopsy for increased PSA levels; this is even more true for those with PSA in the grey zone (4-10 ng/ml) who suffer from lower urinary tract symptoms (LUTS). Such reluctance is likely associated to the perception of most PCas in the elderly being clinically insignificant.

Multiparametric magnetic resonance imaging (mpMRI) of the prostate is increasingly been used in the assessment of patients at risk of being diagnosed with PCa

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given its postulated ability to identify such neoplasm, particularly high-grade disease [1].

The diagnosis of PCa however relies on prostate biopsy (PBx) but the diagnostic yield of Transrectal Ultrasound (TRUS) guided PBx remains low. In current clinical practice the cancer detection rate (CDR) of a first extended TRUS-guided systematic PBx prompted by an elevated PSA level and/or an abnormal digital rectal examination (DRE) is in the range of 40% [2], dropping to approximately 25% in the setting of screening programs, *i.e.* patients with serum PSA between 2.5 and 10 ng/mL [3]. Efforts to improve the diagnostic yield of PBx have been oriented towards the construction of predictive models combining serum PSA and DRE findings with other readily available clinical information such as age, prostate volume (PVol), %freePSA etc., but also towards the development of novel tools including biomarkers [4] and imaging techniques. mpMRI findings seem to increase the accuracy of models predicting PBx outcome [5]. Most important, the possibility of fusing mpMRI and TRUS images to guide PBx, the so-called fusion PBx, has been suggested to significantly increase significantly PBx CDR [6]. The optimal clinical application of mpMRI, however, remains under investigation. According to current EAU guidelines [7], despite the use of the new PIRADS v2 scoring system, mpMRI has a low specificity, with high rates of false positives, especially among lesions scored 3/5 and 4/5. Moreover, the inter-reader reproducibility is moderate, limiting its broad use outside expert centres. Having said this, EAU guidelines recommend it before repeat biopsy (evidence level 1°; grade A). In the present study we evaluated our experience with mpMRI/TRUS fusion-guided PBx comparing its outcome with that of "standard" systematic TRUS guided PBx in the setting of both first and repeat PBx.

PATIENTS AND METHODS

Data of patients scheduled for TRUS-guided transrectal PBx because of increased serum PSA (≥ 4 ng/mL) and/or abnormal digital rectal examination (DRE) were prospectively entered into our dedicated Institutional Review Board-approved database. The present study is a retrospective comparison of the first 99 patients having undergone mpMRI/TRUS fusion-guided PBx (Group A) with a matched population of patients having undergone standard TRUS-guided PBx (Group B) in the same period.

MpMRI was carried out using Intera Achieva by Philips with 1.5 tesla magnetic field strength, in T2WI, DWI axial at 3 b values and DCE-MRI (3Dt1W-THRIWE).

PBx was carried under local non-infiltrative anesthesia [8 9]. TRUS was used to determine prostate and transition zone volume and to guide transrectal prostate sampling according to our systematic 18-core biopsy scheme [10]. In Group A, care was taken to identify the position of the index lesion(s) within our 18-core scheme and to take 2 cores from it using the Navigo™ Workstation (UC-CARE Medical System).

Two senior uropathologists blind to procedural data evaluated the specimens according to contemporary diagnostic criteria for high-grade prostatic intraepithelial neoplasia (HGPIN), atypical small acinar proliferation (ASAP) of prostate [11], and PCa.

The study protocol was approved by the University of Foggia Ethics Committee and was carried out in agreement with the provisions of the Declaration of Helsinki. Written informed consent to take part was given by all participants.

Statistical analysis

Continuous variables were compared by the Mann-Whitney U-test. Rates were tested by the Fisher's exact test or the chi-square test, as appropriate. Statistical significance was set at $p < 0.05$. Statistical calculations were carried out using STATA-SE software, version 14.0 for Mac OS X.

RESULTS

Table I reports the baseline characteristics of the 99 patients having undergone mpMRI/TRUS fusion-guided PBx (Group A) and those of a matched population of patients having undergone standard systematic TRUS-guided PBx (Group B). The percentage of patients aging > 75y was 20% in Group A and 17% in Group B. Procedural time was 37 ± 5.1 min in Group A and 11 ± 1.7 min in Group B ($p < 0.001$); there was no difference in complications rate (Group A 4% *vs* Group B 3%).

The overall CDR (Tab. II) was 60.6% in Group A and 29,2% in Group B $p < 0,001$) whereas the rate of clinically-significant (csPCa), defined as cancers with Gleason sum ≥ 7 [6], was 26.2% in Group A and 13.1% in Group B ($p = 0.02$). In the setting of first PBx, the overall CDR was 76% in Group A and 31.9% in Group B ($p < 0.001$) whereas the rate of csPCa was 34.7% in Group A and 18.6% in Group B ($p = 0.08$). In the setting of repeat PBx, the overall CDR was 47.1% in Group A and 26.9% in Group B ($p = 0.032$) whereas the rate of csPCa was 18.8% in Group A and 8.9% in Group B ($p = 0.132$).

CDR correlated well with the Prostate Imaging-Reporting and Data System (PIRADS), being 50, 61.8 and 90% for PIRADS 3, 4 and 5 respectively in the overall population, specifically 84.6, 67.8 and 100% in the setting of first PBx, and 28.5, 55.5 and 80% in the setting of repeat PBx (Tab. III).

Table I. Patients descriptive characteristics.

	Group A = 99pts	Group B = 99 pts	P-value
AGE (y)	65.6 (58.6 ± 72.6)	66.4 (64 ± 68.8)	0.4958"
PSA (ng/ml)	7.9 (4.9 ± 10.9)	7.3 (4.7 ± 9.9)	0.1558"
Suspicios DRE (%)	33.3 % (33/99)	33.3 % (33/99)	1*
Prostate Volume (mL)	56.4 (30.8 ± 82)	55,1 (32.7 ± 77.5)	0.4811"
Previous PBx (%)	52.5% (52/99)	52,5% (52/99)	1*
Previous Surgery for BPH (%)	3% (3/99)	3% (3/99)	1*

Group A: mpMRI/TRUS fusion guided PBx; Group B: standard TRUS guided PBx.
Data are expressed as means ± standard deviations or percentages. "Student's t-test; * Fisher's exact test.

Table II. Cancer detection rates.

	Group A = 99 pts	Group B = 99 pts	P-value
All Pca	60.6 % (60)	29.2 % (29)	< 0.001
First PBx	76%	31.9%	< 0.001
Repeat PBx	47.1%	26.9%	0.032
csPCa	26.2 % (26)	13.1 % (13)	0.02
First PBx	34.7% (16/46)	18.6% (8/43)	0.08
Repeat PBx	18.8%	8.9%	0.132

Group A *vs* Group B; chi-square test.

Table III. Cancer detection rates by prostate imaging-reporting and data system (PIRADS) version 1 in patients having undergone mpMRI/TRUS fusion guided PBx.

	Overall	First PBx	Repeat PBx	P-value
PIRADS 3 (%)	17/34 (50 %)	11/13 (84.6%)	6/21 (28.5%)	0.001
PIRADS 4	34/55 (61.8 %)	19/28 (67.8%)	15/27 (55.5%)	0.35
PIRADS 5	9/10 (90%)	5/5 (100%)	4/5 (80%)	0.29
Overall	60/99 (60.6 %)	35/46 (76%)	25/53 (47.1%)	0.001

Complications were always minor. Macroscopic hematuria was observed in 2 (2%) cases and lasted 1-2 days. Rectal bleeding were also seen in 2 cases (2%). In one it required endoscopic clipping of a small artery, in the other Foley catheter balloon compression. There was one urinary tract infection which required specific antibiotic treatment. In 2 cases (2%) vasovagal symptoms as sweating, nausea, paleness, dizziness, and hypotension were observed. In all patients, these symptoms regressed when the patient was laid in the Trendelenburg position. Two patients (2%) suffered acute urinary retention treated by an indwelling Foley catheter for one week. All complications occurred in patients > 75y. Like for other procedures [12], the limited number of complications may be linked to our case volume.

DISCUSSION

The present study pointed out that mpMRI/TRUS fusion-guided PBx provided greater CDR than standard systematic PBx for overall PCa and csPCa in the setting of first and repeat PBx. Considering that this was our initial experience (first 99 cases) findings were quite satisfactory. Indeed, it has been reported that such results can be expected after having completed the learning curve of both radiologists and urologists with this procedure. Panebianco et al. [13] reported a learning curve of approximately 50 cases whereas Canio et al. [14] reported a learning curve of 270 cases. Furthermore, we recorded a very satisfactory correlation between PI-RADS scoring and CDR at PBx, somehow challenging the reported mpMRI low specificity and high rates of false positives between PIRADS 3 and 4 lesions [15].
Back to mpMRI indications, EAU guidelines recommend mpMRI before repeat biopsy (evidence level 1°; grade A) whereas its use in candidates for first PBx remains controversial. The initial and simplest method for mpMRI-targeted biopsy strategy is the cognitive approach. Three RCTs have compared a TRUS-guided

12-core PBx with a cognitive mpMRI-guided PBx in the setting of first PBx yielding conflicting results [16-18]. The first two studies pointed out that CDR was higher in the mpMRI-guided group [17 18], whereas the most recent one showed that the two procedures provided comparable results [17].

The mpMRI/TRUS fusion software has been developed with the aim of providing a more precise sampling of the lesions identified by mpMRI. Initial non-randomized studies comparing mpMRI/TRUS fusion PBx with "standard" TRUS-guided PBx in the setting of first PBx pointed out that fusion PBx provided better CDR than "standard" PBx [19 20]. The first RCT comparing mpMRI/TRUS fusion guided PBx with "standard" 12-core TRUS-guided PBx in the setting of first PBx (6) pointed out that "fusion" PBx provided a significantly greater overall CDR than "standard" PBx (50.5 *vs* 29.5%; p = 0.002) and such advantage was even greater for clinically significant PCas (43.9 *vs* 18.1%; p < 0.001).

In the setting of first PBx, our overall CDR was 76% in Group A and 31.9% in Group B (p = < 0,001) whereas the rate of csPCa was 34.7% in Group A and 18.6% in Group B (p = 0.08), thus similar to that achieved by Porpiglia et al. [7]. In the setting of repeat PBx, the overall CDR was 47.1% in Group A and 26.9% in Group B (p = 0.032) whereas the rate of csPCa was 18.8% in Group A and 8.9% in Group B (p = 0.132). Our complication rate was low and consisted of minor events: however, all complications occurred in patients > 75y suffering several comorbidities.

A potential limitation is not having planned a comparison with other tools that have been reported to predict PBx outcome. A commercially available assay combining serum PSA with urinary prostate cancer antigen 3 (PCA3) and the urinary transmembrane protease, serine 2:v-ets erythroblastosis virus E26 oncogene homolog (TMPRSS2: ERG fusion) has been shown to provide a 90% specificity and 80% sensitivity in diagnosing PCa [21]. Similarly, we demonstrated that, in a small cohort of 40 patients scheduled for repeat PBx, Pentraxin 3 significantly outperformed PSA (AUC 0.92 *vs* 0.55) in predicting the risk of being diagnosed with PCa [22]; these findings, however, await validation in a large series of patients scheduled for first PBx.

Another front of research has been addressed towards readily available clinical parameters related to benign prostatic obstruction (BPO). Prostate volume, which is directly correlated to BPO, has been shown to be inversely correlated with the risk of harboring PCa in men scheduled for PBx [23 24]. Being in line with this, we found that, in patients scheduled for PBx because of increased PSA levels and/or abnormal DRE, the International Prostate Symptom Score (IPSS), the peak flow rate (PFR) and the post-void residual (PVR) independently predict the risk of being diagnosed with PCa [25-27]. A novel nomogram based on BPO-related parameters (PFR, PVol, PVR) has recently been shown to predict the risk of prostate cancer at first prostate biopsy with a model predictive accuracy of 0,768 for overall PCa and of 0.8002 for Clinical significant PCa [28]. Question remains whether such clinical factors may impact on the treatment outcome, like smoke in bladder cancer and this is particularly true in elderly patients who present several comorbidities [29].

In conclusions, mpMRI/TRUS fusion-guided PBx provided greater CDR than standard TRUS-guided systematic PBx in the setting of first and repeat PBx. Increasing the CDR of PBx would significantly reduce the number of unnecessary PBxs with significant benefits in terms of costs and patient anxiety. On the other hand, one should take into account the risk of overdiagnosing low-risk PCa, with overtreatment possibly leading to procedure-related complications [30]. Therefore, like for other common benign urological conditions, the final clinical decision has to rely on wise clinical judgment [31-33].

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Conflict of interest

The authors declare no conflict of interest.

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