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ORIGINAL PAPER

Multiparametric MRI targeted prostate biopsy: When omit systematic biopsy?

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Summary ***Introduction: To evaluate the detection rate for prostate cancer (PCa) performing multiparametric magnetic resonance imaging (mpMRI) fusion targeted biopsy (TPBx) combined only with ipsilateral systematic prostate biopsy (SPBx).***
Materials and methods: From January 2023 to December 2023, 495 men with clinical suspicion of PCa underwent transperineal SPBx plus TPBx in the presence of PI-RADS score lesions ≥ 3.
Results: In 250/495 men (50.5%) a PCa was found, while 36/250 (14.4%) men had negative mpMRI. In comparison to TPBx, SPBx diagnosed a higher number of indolent PCa, 38.5 vs. 5.8%, respectively; conversely, SPBx demonstrated a higher detection rate for clinically significant PCa (97.3 vs. 85.4%) in the presence of ISUP Grade Group 2 (GG2). In details, rates were higher in the presence of GG2 (100 vs. 76%), GG3 (85.7 vs. 75.8%) and GG4 (100 vs. 86.4%) tumors. However, in GG5, both SPBx and TPBx diagnosed 100% of csPCa. Furthermore, 89.4% of the cases showed csPCa on the negative mpMRI side.
Conclusions: SPBx combined with TPBx maximized csPCa diagnosis; the use of reduced biopsy scheme limited to ipsilateral side of mpMRI lesion plus TPBx missed 11.6% csPCa. Only in the presence of PI-RADS score 5 SPBx and TPBx diagnosed both 100% of csPCa.

KEY WORDS: Prostate cancer; mpMRI; Targeted biopsy; Systematic biopsy; Gleason score.

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INTRODUCTION

Prostate cancer (PCa) is the most frequent tumor worldwide in the male population (1), with a high estimated risk of overdiagnosis and overtreatment for men enrolled in PSA screening. In the last years, the use of *multiparametric magnetic resonance imaging* (mpMRI) combined with risk calculator including more clinical parameters allowed to improve the diagnosis of *clinically significant PCa* (csPCa) (2-7). In this respect, the diagnosis and treatment of PCa should be tailored for each patient to balance oncological and functional outcomes. Although *Active Surveillance* (AS) protocols (8) have reduced overtreatment of low risk PCa and, in well informed patients, favorable intermediate risk (9, 10) PCa, the necessity of definitive treatment (radical prostatectomy or external radiotherapy) results to worse the quality of life.
Multiparametric MRI has improved the accuracy of systematic prostate biopsy in diagnosing csPCa and reducing unnecessary biopsies; the detection rate for csPCa is correlated with *Prostate Imaging-Reporting and Data System* (PI-RADS) score and in selected cases systematic biopsies could be omitted without harbor PCa diagnosis.
In this study we have prospectively evaluated the detection rate for PCa performing only mpMRI/fusion targeted biopsy combined with ipsilateral systematic prostate biopsy.

MATERIALS AND METHODS

From January 2023 to December 2023, we prospectively evaluated 495 men with clinical suspicion of PCa underwent transperineal systematic (SPBx: 20 cores in both prostatic lobes plus anterior zone) plus mpMRI/transrectal ultrasound (TRUS) fusion biopsy in the presence of PIRADS score lesions ≥ 3 (TPBx: 4 cores) (11, 12).
Clinical criteria for prostate biopsy were: PSA values > 4 ng/ml and/or suspicion *digital rectal examination* (DRE) or revaluation (scheduled biopsy) of men enrolled in AS protocol. After institutional review board and ethical committee approval were granted, the informed consent was obtained from all individual participants included in the study. Median PSA was 7.3 ng/ml (range: 3.8-152 ng/ml), *digital rectal examination* (DRE) was suspicion for PCa in 58/495 (11.7%) cases, 295 *vs.* 200 underwent initial vs. repeated biopsy, 48 men were enrolled in AS protocol for very low/low risk PCa (13). All the mpMRI index lesions characterized by a PI-RADS (version 2) ≥ 3 underwent targeted cores (TPBx: 4 cores); the procedure was performed transperineally using a tru-cut 18 gauge needle (*Bard; Covington, GA, USA*) under sedation and antibiotic prophylaxis. The TPBx was done using an Hitachi 70 Arietta ecograph, Chiba, Japan) supplied by a bi-planar trans-rectal probe (14, 15).
The detection rate for PCa of SPBx in the controlateral "*negative*" mpMRI prostatic lobe of men has been evaluated; in detail, the opportunity to omit systematic biopsy in the hemigland without suspicion mpMRI lesions was evaluated.

RESULTS

None had significant complications (Clavien-Dindo grade I) from prostate biopsy that needed hospital admission;

Table 1.
Biopsy findings in the 250 men with prostate cancer (PCa) submitted to systematic (SPBx) and targeted biopsy (TPBx).

Overall PCa 250	PI-RADS ≤ 2 36 (14.4%)	Positive TPBx	Positive SPBx	PCa only in ipsilateral side	Number of positive cores	Median PSA	GPC median
GG1/GS 6 100 cases	14 (39%)	54 (54%)	96 (96%)	0	2	4.2	25%
GG2/GS 3+4 50 cases	12 (33.3%)	38 (76%)	50 (100%)	2/50 (4%)	8	5.9	40%
GG3/GS 4+3 28 cases	6 (16.6%)	22 (78.5%)	24 (85.7%)	10/28 (35.7%)	10	8.6	55%
GG4/GS 8 26 cases	4 (11.1%)	22 (84.6%)	26 (100%)	2/26 (7.7%)	15	12.5	60%
GG5/GS 4+5 46 cases	0	100%	100%	2/46 (4.3%)	18	19.2	85%

GS: Gleason score; PSA: Prostate specific antigen; GPC: greatest percentage of cancer; PI-RADS: Prostate Imaging-Reporting and Data System; GG: ISUP Grade Group; mpMRI: multiparametric magnetic resonance image

no patient had bilateral suspicious lesions at mpMRI. In 250/495 (50.5%) men a PCa was diagnosed: 100 (40%) had an International Society of Urological Pathology (16) Grade Group 1 (ISUP GG1)/Gleason score 6, 50 (20%) a GG2/Gleason score 3+4, 28 (21.4%) a GG3/Gleason score 4+3, 26 (15.4%) a GG4/Gleason score 8 and 46 (18.4%) a GG5/Gleason score 9. 36/250 (14.4%) men had negative mpMRI (PI-RADS score < 2): 38.9% (14 cases) were GG1, 33.3% (12 cases) GG2, 16.7% (6 cases) GG3, 11.1% (4 cases) GG4, and 0% GG5.

SPBx in comparison with TPBx diagnosed a greater number of indolent PCa equal to 96/250 (38.5%) *vs.* 14/250 (5.8%) men; on the contrary, SPBx showed an higher detection rate for csPCa (97.3 *vs.* 85.4%). In details, rates were higher in the presence of GG2 (100 *vs.* 76%), GG3 (85.7 *vs.* 78.5%) and GG4 (100 *vs.* 84.6%), whereas in GG5 SPBx *vs.* TPBx diagnosed both 100% of csPCa (Table 1). SPBx in comparison with TPBx diagnosed 146/150 (97.3%) *vs.* 128/150 (85.4%) csPCa, respectively.

In total 16/150 (10.6%) men with csPCa had positive systematic cores located only in the ipsilateral side of suspicious mpMRI. Out of them, 2/50 (4%) men with GG2 had PI-RADS 3; 10/28 (35.8%) with GG3 had PI-RADS score 3 (2 cases), 4 (6 cases) and 5 (2 cases), respectively; 2/26 (7.7%) and 2/46 (4.3%) with GG4 and GG5 had lesions PI-RADS score 4, respectively (Table 1).

Performing only TPBx would have spared 14.4% (36/250) biopsies and adding systematic cores in the ipsilateral side of TPBx 11.6% csPCa located in the controlateral prostatic lobe with negative mpMRI would have missed.

Discussion

The use of mpMRI has increased the diagnosis of csPCa with a false negative rate equal to 15-20% of the cases; therefore, systematic biopsies, still today, should be combined with targeted cores to improve PCa diagnosis (17). It remains unknown whether csPCa is missed due to the limited sensitivity of MRI, the suboptimal image fusion, the biopsy technique and strategy, expertise of the surgeon or a combination of these. If the diagnosis of PCa is based on "*MRI pathway*" (18) the patients should be advised of false negative rate for csPCa but, at the same time, the morbidity of the procedure could result less invasive because the lower number of needle cores.

Recently, a reduced-core prostate biopsy strategy confined to the ipsilateral emigland of suspicious mpMRI including "*perilesional cores*" has been proposed to decrease the number of systematic cores, but, still today, the literature data are not in agreement and the detection rate for csPCa is correlated to different PI-RADS scores (19). *Bourgeno et al.* (20) in 2.387 men submitted to different prostate biopsy schemes reported that the added value of contralateral systematic biopsy was negligible in terms of cancer detection (6.1% of the cases) and upgrading rates. *Hegens et al.* (21) reported in 235 patients that TPBx plus-perilesional biopsy approach detected 96.8% csPCa reducing the diagnosis of indolent PCa in 12.8% of the cases. *Deniffel et al.* (22) in 745 men submitted to mpMRI TPBx plus systematic biopsy reported that standard cores could be avoided only in men with PI-RADS score 5 and/or previous negative biopsy, missing 1 *vs.* 2% of csPCa and avoiding 27 *vs.* 58% of systematic procedures. On the other hand, *Sawhney et al*. (23) reported in 490 men that about 20% of men with unilateral MRI lesions and csPCa on targeted biopsy were found to have controlateral csPCa on systematic biopsies. *Phelps et al.* (24) in 212 men with mpMRI-visible intraprostatic lesions demonstrated that TPBx alone diagnosed 81.5% PCa, on the contrary 7.6% had controlateral involvement and 10.9% had bilateral PCa and concluded that TPBx combined with systematic biopsies maximizes csPCa diagnosis. *Hou et al.* (25) in 229 patients showed that the benefit of systematic biopsy added to TPBx was restricted to smaller PI-RADS score 3-4 resulting not useful for the diagnosis of csPCa in the presence of PI-RADS score lesions 5 and larger (> 1 cm) PI-RADS score 3-4 allowing to reduce systematic biopsies in 44.5% of the cases without compromising csPCa diagnosis. The discordant data reported in literature are, probably, correlated with the clinical parameters (DRE, clinical stage, PSA values), PI-RADS score values and number of needle cores performed by systematic prostate biopsy; in general, only in the presence of PI-RADS score 5 controlateral SPBx could be omitted. Anyway, omitting controlateral SPBx a relevant number of csPCa could be definitively missed especially in men candidate to radiotherapy. Recently, new prostate targeted strategies have been proposed; the use of transrectal microultrasound (26) and PSMA PET/CT (27-30) demostrated good accuracy in diagnosing csPCa performing targeted biopsy when compared with mpMRI accuracy, but the results were obtained in men enrolled in clinical trials and/or in limited number of cases.

In our series, among 250/495 (50.5%) PCa 150 (60%) where csPCa and 36 (14.4%) had negative mpMRI (PI-RADS score ≤ 2). SPBx in comparison with TPBx diagnosed a greater number of indolent PCa (38.5 *vs.* 5.8%);

on the ther hand, SPBx showed an higher detection rate for csPCa (97.3 *vs.* 85.4%).
In detail, only 16/150 (10.6%) men with csPCa had positive cores located only in the ipsilateral side of suspicious mpMRI: 2/50 (4%) men with GG2; 10/28 (35.8%) with GG3; 2/26 (7.7%) and 2/46 (4.3%) with GG4 and GG5, respectively. Only men with PI-RADS score 5 had a detection rate for csPCa equal to 100% performing TPBx vs. SPBx (Table 1). TPBx combined with ipsilateral SPBx alone would have missed 27.2% of PCa irrispective of PI-RADS score and 11.6% were csPCa; in addition, quantitative histological findings useful for local staging of PCa and planification of definitive treatment (i.e. nerve sparing prostatectomy; intensity modulated radiotherapy) would have missed. Finally, performing only TPBx would have spared 14.4% biopsies missing the presence of csPCa also in the negative mpMRI side in 89.4% of the cases.
Regarding our results, some consideration should be done. First, PCa diagnosis has been evaluated in biopsy finding and not in the entire prostate specimen; secondly, many patients had an indolent PCa because included in AS protocol and in these cases SPBx combined with TPBx is highly recommended. Finally, a greater number of patients should be evaluated.

Conclusions

SPBx combined with TPBx maximized csPCa diagnosis; the use of reduced biopsy scheme limited to TPBx plus ipsilateral systematic cores missed 11.6% of csPCa; only in the presence of PI-RADS score 5 SPBx and TPBx diagnosed all csPCa.

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