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Research Article

Rebiopsy rate after transperineal or transrectal prostate biopsy

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ABSTRACT

Background: In recent years, transperineal biopsies gained popularity for prostate cancer diagnosis; lower infective complications and improved sampling of the prostate are the main advantages of this technique. One question that remains unclear is whether an initial transperineal biopsy confers a lower risk for rebiopsy compared with the transrectal approach.
Methods: Six hundred seventy-one men were prospectively followed after an initial negative prostate biopsy for a median period of 49.50 (IQR: 37.62–61.17) months. Rebiopsy rate was analyzed attending to first biopsy approach (transrectal versus transperineal systematic) and clinical variables.
Results: Diagnostic rate was similar for transrectal and transperineal systematic biopsies. Targeted biopsies outperformed any systematic approach, and transperineal targeted in particular was superior to transrectal targeted. Rebiopsy rates were 15.4% and 5.26% for the transrectal and transperineal systematic groups, respectively. Prostate-specific antigen density and type of first biopsy were identified as rebiopsy predictors.
Conclusion: Men undergoing transperineal systematic biopsies had a three times lower rate of rebiopsy over the study period compared with the traditional transrectal approach. This advantage could be added to the already described potential benefits of transperineal biopsies. Targeted biopsies had lower rebiopsy rate over the study period. Further innovations that decreased the cost of transperineal biopsies could favor this approach in the future.

1. Introduction

Prostate cancer (PCa) diagnosis is based on histopathological examination of prostate biopsy cores.[1] Two main routes have been described to obtain prostate cores: transrectal ultrasound guided prostate biopsy (TRUSBx) or transperineal prostate biopsy (TPBx). The first is performed puncturing the rectal wall to reach the prostate with the inherited risk of prostatitis and severe sepsis, as well as severe rectal bleeding.[2] The transperineal approach gains access to the prostate through the perineal skin and pelvic floor muscle, which reduces risk of infections,[3] and allows better sampling of the prostate reaching anterior and apical sectors of the prostate and improves registration of MRI targets.[4–6]

Despite the diagnostic yield of both techniques is comparable,[7] TPBx confers a more accurate representation of the entire PCa burden compared with the transrectal approach;[8] this is paramount when considering conservative PCa approaches such as focal therapy or active surveillance.[9]

One question that, to our knowledge, remains unclear is whether the rebiopsy rate due to suspicion of significant PCa is any different after an initial transrectal or transperineal negative prostate biopsy.

To address this, we retrospectively reviewed our database on PCa diagnosis focusing in detecting differences in rebiopsy rates after an initial negative transrectal or transperineal systematic prostate biopsy in a single high-volume center.

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2. Material and methods

2.1. Patient characteristics

One thousand two hundred forty-five men with suspected PCa underwent an initial prostate biopsy between 2014 and 2019 at our institution. All men underwent an ultrasound in clinic to assess prostate volume; a cutoff point of 60 cc was used to offer transrectal prostate biopsy for smaller prostates and transperineal otherwise. From 2017 onwards, all men referred for suspected PCa received routine prebiopsy MRI. When a suspicious MRI target was identified, a transrectal or transperineal targeted biopsy (cognitive or software fusion) was offered; in all targeted approaches, systematic biopsies were also taken.

Transrectal biopsy was performed in office under local anesthesia, an ultrasound probe was inserted to scan the prostate, and a 20G biopsy needle was used to obtain 12–18 cores. Transperineal biopsies in turn were performed in theaters; under general or spinal anesthesia, the patient was placed in lithotomy position and an ultrasound probe mounted on a stabilizer was inserted in the rectum. A grid was used to guide a 20G biopsy needle; 30 cores were obtained to sample all areas of the prostate.

For analysis purposes, biopsies were grouped in transrectal systematic, transrectal targeted, transperineal systematic, and transperineal targeted. In all targeted biopsies, a systematic mapping was also performed. For the purpose of this study, we focused on systematic-only biopsies; targeted biopsies were excluded.

The first biopsy approach and outcomes are summarized in Table 2; demographic data are represented in Table 3. Overall, 671 (70.71%) patients had an initial negative biopsy result and were followed with further yearly prostate-specific antigen (PSA) surveillance, digital rectal examination, and prostate MRI. Repeat biopsy was indicated if PCa suspicion was high, despite initial negative biopsy following our own protocol shown in Table 1 and obtained from previous multivariate models (data not shown). Rebiopsy was indicated for scores 2 or greater. This clinical and biomarker panel was optimized clinically with the information of mpMRI when performed, but it has not been incorporated into our nomograms thus far.

2.2. Study analysis

The Chi-square test was used to compare categorical variables. To compare continuous variables, the Student *t* test was used when normality could be accepted and the U Mann–Whitney test otherwise.

When feasible, Cox proportional hazards regression models were applied to evaluate rebiopsy predictors. Step function was used to select the best model according to the Akaike information criterion.

Table 1
Rebiopsy protocol: rebiopsy was indicated for scores 2 or greater.

Variable	Value	Score
PSA	>10 ng/ml	+1
PSA velocity	>1 ng/ml/year	+1
Prostate volume	<50 cc	+1
PSA free/PSA	<0.15	+1
PCA3	>35	+1
First degree familiar history of PCa	Yes	+1
Prostatitis	Yes	−1

PCA3: prostate cancer antigen 3; PSA: prostate-specific antigen; PCa: prostate cancer.

Two-sided tests with a level of significance of 5% were used. Data analysis was performed using R language programming (Vienna, Austria: R Foundation for Statistical Computing; 2018, version 3.6.3).[10]

3. Results

Clinical information is displayed in Table 3; age was similar among all groups. PSA values and prostate volume were significantly higher for the TPBx group. Nevertheless, PSA density (PSAd) was equal for both groups. This is due to bigger prostates being preferably selected for TPBx. Despite this, PSAd was similar among groups, suggesting that both groups were comparable regarding this relevant variables.

99.6% and 98.7% of TRUS and TP systematic biopsies, respectively, did either not receive a prebiopsy MRI or had a negative result.

There was no difference in the diagnostic yield for systematic initial TRUS or TP systematic Bx (29.23% and 30%, respectively). Targeted biopsies showed a better diagnostic performance than systematic (54.07% and 67.82% for transrectal and TP targeted, respectively) (Table 2). Targeted transperineal had a greater diagnostic rate than transrectal targeted ($p = 0.04$).

There was no difference in the rate of significant PCa detection defined as any Gleason grade greater than 6.

Of all, 15.4% and 5.26% of patients from the transrectal ultrasound guided prostate biopsy and TP systematic groups, respectively, underwent a rebiopsy during the study period. The univariate Cox regression model identified PSAd as an independent predictor of rebiopsy; the type of biopsy did not show a statistically significant difference ($P = 0.061$) but a tendency was observed for a lower rebiopsy rate in the TP biopsy group. In the multivariate analysis, PSAd and type of biopsy were identified as predictors of rebiopsy, and the TP approach conferred a lower rebiopsy rate compared with transrectal (HR: 0.275; CI 95%: 0.086–0.884) (Table 4).

4. Discussion

There is a current debate advocating for a change form the gold standard diagnostic approach of transrectal prostate biopsy to a transperineal approach.[11] This is based on the potential advantages of TPBx, namely a noninferior diagnostic rate, arguably superior for anterior tumors, and reduction in infective complications.[12] Furthermore, in this prospective evaluation, we observed a threefold reduction in the number of men undergoing a second biopsy over a 4-year period which could be added to the potential benefits of this approach. This could be due to the more extensive sampling of the prostate in the first instance and should also be taken into account in cost-effectiveness studies.

The deterrent stopping widespread implementation of transperineal biopsy is the increased cost due to the need for anesthesia and specialized equipment. To alleviate this, transperineal biopsy under local anesthetia using a grid stepper has been described.[13] More recently, a less invasive approach to perform freehand transperineal biopsies under local anesthetia through two parallel access points has been reported. This technique also reduces the costs of the procedure as no special equipment is required.[14,15]

To summarize, transperineal prostate biopsies confer lower infective complications and better sampling of the entire prostate gland. In this study, we observed a lower rebiopsy rate after a first negative systematic biopsy compared with the traditional transrectal approach. Given the present debate advocating switching from the transrectal to transperineal approach, this decrease in number of biopsies and thus in cost should be considered.

Table 2
Type and results of first biopsy.

First biopsy approach	First biopsy result		Total	p-value
	Negative	Positive		
TRUSBx	615 (70.77%)	254 (29.23%)	869 (69.80%)	<0.001
TPBx	56 (70.00%)	24 (30.00%)	80 (6.43%)	
TRUSBx targeted	96 (45.93%)	113 (54.07%)	209 (16.79%)	
TPBx targeted	28 (32.18%)	59 (67.82%)	87 (6.99%)	
Total	**795 (63.86%)**	**450 (36.14%)**	**1245 (100.00%)**	

TRUSBx: transrectal ultrasound guided prostate biopsy; TPBx: transperineal prostate biopsy.

Table 3
Clinical and demographics data of the study cohort.

Variable	Total	First biopsy approach		P-value
		TRUS	TP	
	671 (100%)	615 (91.65%)	56 (8.35%)	
Age				0.262
Mean (SD)	63.23 (6.70)	63.15 (6.77)	64.09 (5.89)	
Median (IQR	63.49 (58.40–68.42)	63.46 (58.22–68.35)	64.09 (60.13–68.95)	
PSA				<0.001
Mean (SD)	5.15 (3.16)	4.82 (2.51)	8.71 (6.10)	
Median (IQR)	4.35 (3.43–5.71)	4.27 (3.40–5.50)	6.97 (4.47–12.00)	
Prostate volume				<0.001
Mean (SD)	51.22 (25.74)	49.48 (24.81)	70.35 (28.24)	
Median (IQR)	45.00 (33.00–63.40)	44.00 (32.00–60.18)	71.45 (45.75–84.00)	
PSAd				0.293
Mean (SD)	0.12 (0.08)	0.12 (0.08)	0.13 (0.08)	
Median (IQR)	0.10 (0.07–0.15)	0.09 (0.07–0.14)	0.11 (0.07–0.16)	
Follow-up time				<0.001
Mean (SD)	47.31 (17.07)	49.16 (15.80)	27.01 (17.41)	
Median (IQR)	49.50 (37.62–61.17)	50.64 (38.95–61.87)	20.70 (17.81–40.98)	

PSA: prostate-specific antigen; PCa: prostate cancer; PSAd: prostate-specific antigen density; TR: transrectal biopsies; TP: transperineal biopsies; SD: standard deviation.

Table 4
Univariate and multivariate Cox regression models.

Variable	Total	Rebiopsy		Univariate			Multivariate by STEP function		
		No	Yes	HR	CI: 95%	P-value	HR	CI: 95%	P-value
	671 (100%)	573 (85.39%)	98 (14.61%)						
Age				0.974	0.946–1.003	0.079	0.9744	0.946–1.004	0.090
Mean (SD)	63.23 (6.70)	63.42 (6.70)	62.14 (6.65)						
Median (IQR)	63.49 (58.40–68.42)	63.81 (58.52–68.75)	62.34 (57.38–66.47)						
PSA				1.046	0.995–1.100	0.076			
Mean (SD)	5.15 (3.16)	5.07 (3.06)	5.62 (3.68)						
Median (IQR)	4.35 (3.43–5.71)	4.27 (3.42–5.68)	4.70 (3.68–6.23)						
PSAd				34.400	6.934–170.665	**<0.001**	60.378	11.470–317.822	**<0.001**
Mean (SD)	0.12 (0.08)	0.11 (0.07)	0.15 (0.12)						
Median (IQR)	0.10 (0.07–0.15)	0.09 (0.07–0.14)	0.11 (0.08–0.18)						
Prostate volume				0.996	0.988–1.005	0.389	1.007	0.998–1.015	0.110
Mean (SD)	51.22 (25.74)	51.60 (24.89)	48.99 (30.29)						
Median (IQR)	45.00 (33.00–63.40)	46.00 (33.40–65.00)	40.08 (30.13–56.50)						
First biopsy approach									
TRUSBx	615 (91.70%)	520 (84.55%)	95 (15.45%)	(baseline)			(baseline)		
TPBx	56 (8.30%)	53 (94.64%)	3 (5.36%)	0.334	0.106–1.053	0.061	0.275	0.086–0.884	**0.030**

PSA: prostate-specific antigen; PCa: prostate cancer; PSAd: prostate-specific antigen density; TRUSBx: transrectal ultrasound guided prostate biopsy; TPBx: transperineal prostate biopsy; CI: confidence interval; HR: Hazard risk; IQR: interquartile rank; SD: standard deviation. Bold value reflects a statistical significance.

Source of finding

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Conflicts of interest

All authors have no conflict of interest to declare.

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