Prostate biopsy approach and complication rates

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Abstract. Prostate biopsy is the gold standard to confirm prostate cancer. In addition to standard 12-core biopsies, magnetic resonance imaging (MRI)-guided prostate biopsies have recently been introduced to improve the detection of clinically significant prostate cancer. The present study aimed to compare the complications after standard transrectal ultrasound-guided and standard plus targeted (MRI-guided) prostate biopsies, to study the impact of the number of biopsy cores on complication rates, and to compare complication rates after transrectal ultrasound-guided prostate biopsies with those following transperineal prostate biopsies from the literature. A prospective study was performed, which included 135 patients who underwent transrectal ultrasound-guided prostate biopsies between April 1 and June 30, 2022, at the Urology Department of the University Hospital of Pointe à Pitre (Pointe à Pitre, Guadeloupe). A total of 51 patients were excluded because of missing information concerning their post-biopsy surveillance. The median age at the time of biopsy was 69 years, median prostate-specific antigen value was 8.9 ng/ml, median prostate volume was 57.5 ml, and median number of cores was 15. A total of 35 of the 84 included patients (41.7%) had a standard biopsy only and 49 (58.3%) had targeted (MRI-guided) plus standard biopsies. A total of 53 patients (63.1%) experienced early side effects, whereas only 24 patients (28.6%) experienced late side effects. Three patients (3.6%) required hospitalization for post-biopsy complications. Early side effects, especially hematuria and hematospermia, occurred significantly more frequently in the targeted plus standard group, with more cores taken, with no significant difference concerning late side effects or infectious complications between the standard and standard plus targeted groups. The admission rate for sepsis after transperineal biopsy has been reported to vary between 0 and 1%, whereas the present study had an admission rate of 2.29% using the transrectal approach. Further studies are required to analyze the complications requiring hospitalization after transrectal and transperineal biopsies.

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Introduction

Prostate cancer is among the most common cancers of men. Prostate biopsy is the gold standard technique to diagnose prostate cancer. It is performed either transrectally or by a transperineal approach. Recently, magnetic resonance imaging-(MRI)-guided biopsies have started to be used for targeted biopsies to improve the detection rate of clinically significant prostate cancer (1).

Transrectal ultrasound scan-(TRUS)-guided prostate biopsy is the most commonly used technique, in which 12 cores are generally taken. With the introduction of MRI-guided prostate biopsy, a standard 12-core biopsy plus a targeted biopsy of suspicious areas is often performed on biopsy-naïve patients.

There has been a notable increase in the infectious complication rates after prostate biopsies using the transrectal approach. Thus, there is a growing interest in the transperineal approach for the histological diagnosis of prostate cancer.

A recent multi-institutional study showed that the use of transperineal MRI-targeted prostate biopsy increased the detection of clinically significant prostate cancer (csPCa) relative to transrectal MRI-targeted prostate biopsy, in particular, for cancers located in the apex, transition/central zone, and anterior zone (2).

We aimed to compare the complications after standard transrectal ultrasound-guided and standard plus targeted (MRI-guided) prostate biopsies and study the impact of the number of biopsy cores on the complication rate.

Materials and methods

Study population. We performed a prospective study that included 135 patients who underwent transrectal ultrasound-guided prostate biopsies from April 1 to June 30, 2022, at the Urology Department of the University Hospital of Pointe à Pitre, Guadeloupe. The inclusion criteria were: Male, >18 years, all patients who were scheduled to undergo prostate biopsy for suspected prostate cancer as part of their regular medical care (elevated PSA and/or suspicious DRE and/or suspicious lesion at the mpMRI), patients eligible for transrectal ultrasound-guided prostate biopsies. The exclusion criteria were: <18 years, impaired mental status, patients with no access to rectum, patients whose procedure required general anesthesia. The data collection took place between the 1st of April and 15th of July 2022. The approval of the Institutional Review Board of the University Hospital of Pointe à Pitre, Guadeloupe and the registration for the present study was obtained according to the institution's policy to collect the necessary information from the system (approval no. 2229813).

Protocol. We used the Koelis system for the standard and MRI-guided transrectal prostate biopsies. Prostate biopsies were performed transrectally in an outpatient setting under local anesthesia (10 ml 2% xylocaine, injection of 5 ml on each side of the prostate). Antibiotic prophylaxis was systematically used before prostate biopsy and consisted of fluoroquinolones (400 mg of ofloxacin) 2 h before the procedure. Rectal preparation was performed using Normacol the day before and 3 h before the biopsy. For MRI-guided transrectal prostate biopsies we routinely take three cores per suspicious target, in addition to the standard 12 cores, to improve the detection of clinically significant prostate cancer. Two weeks after the prostate biopsy, patients were phoned to collect information concerning possible complications during the post-biopsy period. Among post-biopsy complications, early side effects were defined as hematuria, rectal bleeding, hematospermia, sepsis, and/or acute urinary retention between day 0 and day 2 and late side effects as hematuria, rectal bleeding, hematospermia, sepsis, and/or acute urinary retention between day 3 and day 15.

Statistical analyses. Fifty-one patients were excluded because of missing information concerning their post-biopsy monitoring, including 10 for prostate volume.

We used the chi-squared test or Fisher's exact test for categorical variables, Mann-Whitney tests for comparisons of the medians, and unpaired t-test (equal variances) for continuous variables. We also used logistic regression analysis to estimate the odds ratios (ORs) and 95% confidence intervals (CIs) for associations between risk factors of side effects and biopsies. All statistical analyses were carried out using Statview software (SAS Institute, Cary, NC). All tests were two-tailed and $P<0.05$ was considered to indicate a statistically significant difference.

Table I. Characteristics of the population.

Variable	Value
Number of patients (%)	84 (100)
Median age at biopsies, years (range)	69.0 (48.0-93.0)
Median PSA at biopsies, ng/ml (range)	8.9 (0.2-1,931.0)
Median prostate volume, cc (range)	57.5 (4.0-183.0)
Median number of biopsy cores (range)	15 (6-22)
Type of biopsy (%)	
Standard only	35 (41.7)
Targeted + standard	49 (58.3)
Anticoagulant therapy (%)	
No	75 (89.3)
Yes	9 (10.7)
Urinary infection history (%)	
No	83 (98.8)
Yes	1 (1.2)
Diabetes (%)	
No	68 (81.0)
Yes	16 (19.0)
Early side effects, day 0-day 2 (%)	
No	31 (36.9)
Yes	53 (63.1)
Late side effects, day 3-day 15 (%)	
No	60 (71.4)
Yes	24 (28.6)
Complications requiring hospitalization (%)	
No	81 (96.4)
Yes	3 (3.6)

Results

The median age at the time of biopsy was 69 years, median PSA value 8.9 ng/ml, median prostate volume 57.5 ml, and median number of cores 15 (Table I).

Thirty-five of the 84 included patients (41.7%) had standard biopsy only and 49 patients (58.3%) MRI-guided plus standard biopsies. Concerning risk factors, nine patients (10.7%) were under anticoagulant therapy. There was only one patient (1.2%) who had a history of urinary infection. Sixteen patients (19%) were diabetic (Table II).

Concerning complications after biopsy, 53 patients (63.1%) experienced early side effects in the first two days after the intervention (Table III). Only 24 patients (28.6%) experienced late side effects between day 3 and day 15. Three patients (3.6%) required hospitalization for complications post-biopsy (Table IV).

Comparison of the complications after standard transrectal ultrasound-guided and MRI-guided plus standard prostate biopsies showed significantly more early side effects, especially hematuria and hematospermia, after MRI-guided plus standard prostate biopsies than after standard prostate biopsies: 73.5% vs. 48.6%. Concerning late side effects, there

Table II. Characteristics of the population according to the type of biopsy.

Variable	Standard only	Targeted + standard	P-value
Number of patients (%)	35 (41.7)	49 (58.3)	-
Median age at biopsies, years (range)	71.0 (48.0-93.0)	68.0 (55.0-93.0)	0.02
Median PSA at biopsies, ng/ml (range)	12.5 (0.2-1,931.0)	7.2 (3.2-18.7)	<0.001
Median prostate volume, cc (range)	60.0 (4.0-183.0)	55.0 (10.0-125.0)	0.06
Median number of biopsy cores (range)	12 (6-12)	16 (15-22)	0.001
Anticoagulant therapy (%)			0.59
No	32 (91.4)	46 (87.8)	
Yes	3 (8.6)	6 (12.2)	
Urinary infection history (%)			0.40
No	35 (100.0)	48 (98.0)	
Yes	0 (0.0)	1 (2.0)	
Diabetes (%)			0.19
No	26 (74.3)	42 (85.7)	
Yes	9 (25.7)	7 (14.3)	
Early side effects, day 0-day 2 (%)			0.02
No	18 (51.4)	13 (26.5)	
Yes	17 (48.6)	36 (73.5)	
Late side effects, day 3-day 15 (%)			0.33
No	27 (77.1)	33 (67.3)	
Yes	8 (22.9)	16 (32.7)	
Complications requiring hospitalization			0.77
No	34 (97.1)	47 (95.9)	
Yes	1 (2.9)	2 (4.1)	

Table III. Early side effects according to the type of biopsy.

Variable	Standard only	Targeted + standard	P-value
Early side effects, day 0-day 2 (%)			0.02
No	18 (51.4)	13 (26.5)	
Yes	17 (48.6)	36 (73.5)	
Hematuria (%)			0.05
No	21 (60.0)	19 (38.8)	
Yes	14 (40.0)	30 (61.2)	
Hematochezia (%)			0.12
No	31 (88.6)	37 (75.5)	
Yes	4 (11.4)	12 (24.5)	
Hematospermia (%)			0.05
No	31 (88.6)	35 (71.4)	
Yes	4 (11.4)	14 (28.6)	
Sepsis (%)			0.23
No	34 (97.1)	49 (100.0)	
Yes	1 (2.9)	0 (0.0)	
Acute retention of urine (%)			0.40
No	35 (100.0)	48 (98.0)	
Yes	0 (0.0)	1 (2.0)	

Table IV. Late side effects according to the type of biopsy.

Variable	Standard only	Targeted + standard	P-value
Late side effects, day 3-day 15 (%)			0.32
No	27 (77.1)	33 (67.3)	
Yes	8 (22.9)	16 (32.7)	
Hematuria (%)			0.53
No	29 (82.9)	43 (87.8)	
Yes	6 (17.1)	6 (12.2)	
Hematochezia (%)			0.73
No	33 (94.3)	47 (95.9)	
Yes	2 (5.7)	2 (4.1)	
Hematospermia (%)			0.19
No	31 (88.6)	38 (77.6)	
Yes	4 (11.4)	11 (22.4)	
Sepsis (%)			0.40
No	35 (100.0)	48 (98.0)	
Yes	0 (0.0)	1 (2.0)	
Acute retention of urine (%)			0.40
No	35 (100.0)	48 (98.0)	
Yes	0 (0.0)	1 (2.0)	

was a non-significant difference between the two groups: 32.7% for MRI-guided plus standard vs. 22.9% for standard only. The two groups were comparable in terms of the median age (68 years vs. 71 years) and prostate volume (55 cc vs. 60 cc). The median number of cores for the standard group was 12 vs. 16 for the MRI-guided plus standard group. The number of patients who were under anticoagulant therapy was 12.2% in the MRI-guided plus standard group vs. 8.6% in the standard group. There were no significant differences concerning anticoagulant therapy between the two groups. The sample size used in this study was too limited to analyze other risk factors, such as diabetes or history of urinary infection (Table V).

Three patients required hospitalization: one after a standard transrectal prostate biopsy for sepsis and two after an MRI-guided plus standard prostate biopsy for excessive rectal bleeding and sepsis.

Table V. Risk factors of side effects of biopsies.

Variable	Crude OR (95% CI)	P-value
Type of biopsy		0.02
Standard only	1.0	
Targeted + standard	3.33 (1.24-8.93)	
Anticoagulant therapy		0.66
No	1.0	
Yes	1.45 (0.28-7.55)	
Diabetes		0.73
No	1.0	
Yes	1.25 (0.36-4.35)	
Age at biopsies (years)	0.99 (0.94-1.05)	0.86
PSA at biopsies (ng/ml)	1.00 (0.99-1.01)	0.68
Prostate volume (cc)	0.99 (0.98-1.01)	0.48
Number of biopsy cores	1.09 (0.91-1.29)	0.35

Discussion

A systematic review of the literature including eighty-four references was performed to analyze the complications after different prostate biopsy approaches (3). The most frequent complications were hematuria and hematospermia, irrespective of the biopsy approach. The urinary retention rate was higher after transperineal approach (4-11).

In the European Randomized Study for Prostate Cancer (ERSPC) study, the incidence of hematuria lasting more than three days was 22.6% (12). In our study, hematuria lasting more than two days was considered to be a late side effect, for which the incidence was 17.1% for the standard approach and 12.2% for standard plus targeted approach. Data for the impact of the number of cores on hematuria is conflicting. In our study, the number of cores was associated with the rate of early side effects but not that of late side effects.

Ghani *et al* found that the prevalence of hematuria did not vary with the number of cores: 44% for six cores, 41% for eight cores, and 39% for 12 (5). Others reported higher rates of bleeding with an increasing number of cores (13). Pepe and Aragona reported hematuria in 10.4% of patients, regardless of the number of cores (11). Admission to the hospital for severe hematuria was reported in less than 1% of cases (14,15).

The rate of rectal bleeding in the ERSPC study was 1.3% (12). Ghani *et al* found a significantly higher rate of rectal bleeding that correlated with the number of cores (5).

Table VI. Studies reporting hospital admission rates for sepsis after transperineal biopsies.

First author, year	Type of biopsy	Number of patients undergoing biopsy	Hospital admission rate (%)	Number of cores	(Refs.)
Grummet, 2014	Transperineal	244	0	NA	(20)
Vyas, 2014	Transperineal	634	0	24-38	(21)
Tsivian, 2013	Transperineal	84	0	NA	(10)
Namekawa, 2015	Transperineal	2,086	0	NA	(22)
Penzkofer, 2015	Transperineal	90	0	NA	(23)
Panebianco, 2015	Transperineal	23	0	NA	(24)
Kuru, 2013	Transperineal	347	0	N/A	(25)
Pal, 2012	Transperineal	40	0	36	(26)
Suzuki, 2009	Transperineal	539	0	14	(27)
Kubo, 2009	Transperineal	45	0	14	(28)
Merrick, 2008	Transperineal	129	0	24	(29)
Hara, 2008	Transperineal	126	0	12	(30)
Li, 2007	Transperineal	303	0	24	(31)
Pinkstaff, 2005	Transperineal	210	0	21	(32)
Emiliozzi, 2003	Transperineal	107	0	6	(33)
Pepe, 2013	Transperineal	3,000	0,7	12-24	(11)
Symons, 2013	Transperineal	409	1	22	(34)
Ekwueme, 2013	Transperineal	270	1	28	(35)
Dimmen, 2012	Transperineal	69	1	N/A	(36)
Yamamoto, 2005	Transperineal	300	1	12	(37)
Miller, 2005	Transperineal	81	1	6	(38)

Berger *et al* reported a rectal bleeding rate of 2.3% (6). In our study, the occurrence of rectal bleeding was 11.4% in the standard 12-core biopsy group and 24.5% in the standard plus MRI-guided biopsy group in the first two days, of which 5.7% vs. 4.1%, respectively, was a late side effect.

Another common complication, hematospermia, ranged from 1.1 to 92.6%, depending on the study (3,5,7,11,13,16). In our study, we had a rate of 28.6% (standard plus MRI-guided) vs. 11.4% (standard) in the first two days and 22.4% vs. 11.4%, respectively, as a late side effect from day 3 to day 15. Rosario *et al* reported a rate of 92.6% within 35 days after prostate biopsy (8). In the ERSPC study, the rate was 50.4%. They found that the number of cores can have an influence on the rate of hematospermia, regardless of the procedure (12). In the study of Berger *et al*, the median rate was 36.3%, significantly increasing with the number of cores: 31.8% after six cores, 37.4% after 12 cores, and 38.4% after 15 (6). Pepe and Aragona confirmed the correlation between the number of cores and the hematospermia rate (11).

The incidence of acute urinary retention ranged from 0.4 to 6%, depending on the study (3,9,11,17,18). It was 2% in our MRI-targeted plus standard group. In the literature, the occurrence of acute urinary retention has been reported to be slightly higher after the transperineal approach, ranging from 1.7 to 11.1% (3). Pepe and Aragona found that the incidence of acute urinary retention increased with the number of cores taken (11). In our study, we had a single case of acute urinary retention. Thus, we could not study the risk factors for this complication, aside from the fact that it occurred in the MRI plus standard biopsy group, with more cores taken. The volume of the prostate was 109 ml. There were no other risk factors present in this case.

The most troublesome complications after prostate biopsies are infectious complications. To minimize the risk, antibiotic prophylaxis is given before the intervention. It is known that the occurrence of infectious complications is significantly lower after transperineal biopsy, given the avoidance of bacterial contamination (3). In our study, there was one case (2.9%) of sepsis as an early side effect in the standard group and one case (2%) as a late side effect in the standard plus MRI-guided group.

Hospitalization rates have been reported to vary depending on the study according to the approach used for biopsy. In our study, three patients (3.6%) were hospitalized after transrectal prostate biopsy, two because of sepsis and one because of substantial rectorrhagia. In the study of Anastasiadis *et al* from the English National Cancer Registry, the hospitalization rate was 3.7% due to biopsy-related complications. Independent predictors of complications requiring hospitalization were age and comorbidities (19). The retrospective analysis of Nam *et al* reported an overall hospitalization rate of 1.4%, with no significant differences based on age (14). The study Loeb *et al* from the SEER database reported a 6.9% hospitalization rate (4) and the Rotterdam section of the ERSPC a 0.8% hospitalization

rate after prostate biopsy. The hospitalization rate was lower following transperineal biopsies (3).

In the literature, the re-admission rate for sepsis after transperineal prostate biopsies has been reported to be zero in multiple studies Grummet *et al* (20), Vyas *et al* (21), Tsivian *et al* (10), Namekawa *et al* (22), Penzkofer *et al* (23), Panebianco *et al* (24), Kuru *et al* (25), Pal *et al* (26), Suzuki *et al* (27), Kubo *et al* (28), Merrick *et al* (29), Hara *et al* (30), Li *et al* (31), Pinkstaff *et al* (32), Emiliozzi *et al* (33), whereas one found a re-admission rate of 0.7% (11), and several a re-admission rate of 1% (Table VI) (34-38).

Recently, a multicenter retrospective cohort study evaluated MRI-targeted prostate biopsies, comparing targeted transrectal and transperineal biopsies. They found that the transperineal MRI-targeted prostate biopsy approach may increase the detection of clinically significant prostate cancer relative to the transrectal MRI-targeted prostate biopsy approach, in particular, for cancers located in the apex, transition/central zone, and anterior zone (2).

Our study had several limitations, including the small number of patients in the cohort and missing information of the prostate volume in 10 cases, the differences between the baseline characteristics and PSA values between the two groups, and the lack of a transperineal group to compare and evaluate the complications between the standard and standard and MRI-guided group after either the transrectal or transperineal approach.

In conclusion, prostate biopsy is the gold standard for confirming prostate cancer. In our study, we compared the complications between a standard and a standard plus MRI-guided prostate biopsy group. The early side effects, in particular, hematuria and hematospermia, were significantly higher in the targeted plus standard group, with more cores taken, with no significant difference in the late side effects or infectious complications between the two groups. The reported admission rate for sepsis after transperineal biopsy varies between 0 and 1% depending on the study. In our study, we had an admission rate of 2.29%. Other risk factors, such as environment, the experience of the technicians, and the equipment used, which may affect the results, are also worth mentioning. Further studies are required to analyze the troublesome complications requiring hospitalization after transrectal and transperineal biopsies. The choice of the biopsy approach should take into consideration the complication rates and the detection rates of clinically significant prostate cancer.

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Availability of data and materials

The datasets generated and/or analyzed during the current study are not publicly available due to the institution's policy, but are available from the corresponding author on reasonable request.

Authors' contributions

KM, LB, PGV, YS, ML, GS, FM, PB and BI designed the study concept. LB coordinated the study. KM, SN, SB, CB, NG and TC performed the prostate biopsies. LB performed the statistical analysis. KM was responsible for the data collection from the informatical system of the University Hospital of Pointe à Pitre, Guadeloupe, and collected data on the early and late side effects of the patients after the biopsy. FM was responsible for the language editing of this manuscript and helped to write the main manuscript. PGV, YS, ML, GS, PB, BI and LB were involved in planning and supervising the work, and participated in data interpretation KM wrote the manuscript with input from all authors. KM and LB confirm the authenticity of all the raw data. All authors read and approved the final manuscript.

Ethics approval and consent to participate

The approval of the Institutional Review Board of the University Hospital of Pointe à Pitre, Guadeloupe, and the registration for the present study was obtained according to the institution's policy (approval no. 2229813). Written informed consent was obtained before the prostate biopsies. The registered study was allowed to have the patient's oral consent to collect the necessary information concerning the early and late side effects in the first 2 weeks after the prostate biopsies.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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