Feasibilities and outcomes of patients treated with simultaneous prostate biopsy and general urological surgeries

RUI SU[1-4], JIN-FENG PAN[1,5], RUI-DA HUANG[1,5], ZHU-LEI TAO[1,5], CHENG-LING YU[2], JUN-HUI JIANG[2,3] and QI MA[1,2,4,6]

[1]Comprehensive Urogenital Cancer Center, Ningbo First Hospital, The Affiliated Hospital of Ningbo University; [2]Ningbo Clinical Research Center for Urological Disease; [3]Department of Urology, Ningbo First Hospital, The Affiliated Hospital of Ningbo University; [4]Yi-Huan Genitourinary Cancer Group, Ningbo, Zhejiang 315010; [5]Medical School, Ningbo University, Ningbo, Zhejiang 315211; [6]Translational Research Laboratory for Urology, The Key Laboratory of Ningbo City, Ningbo First Hospital, The Affiliated Hospital of Ningbo University, Ningbo, Zhejiang 315010, P.R. China

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Abstract. The present single-center retrospective clinical real-world study aimed to assess the feasibility and outcomes of patients who underwent simultaneous prostate biopsy and general urological surgeries. The medical records of 49 patients who underwent prostate biopsy and general urological surgeries simultaneously from October 2016 to June 2019 were retrospectively reviewed. Patients' outcomes were evaluated 3 days, 1 month and 6 months after biopsy. Of the 49 biopsy cases, 41 were treated by transurethral prostatectomy, two by ureteroscopic lithotripsy, two by laparoscopic renal cyst decortication, two by cystostomy and two by ureteral stent extraction. The overall detection rate of clinically significant prostate cancer was 22.4%. The rate in patients with a prostate imaging reporting and data system (PI-RADS) score of 4-5 was 100%, while in cases with a PI-RADS score of <3 it was 7.1%. Postoperative complications within 3 days included hematuria in 39 (79.6%) cases, fever in three (6.1%) cases and hematochezia in two (4.1%) cases. There was no significant difference in the incidence of hematuria between the transrectal and transperineal approaches; however, the overall incidence of complications was significantly reduced after switching from a transrectal approach to a transperineal approach. No complications were observed after 1 or 6 months. In summary, combining simultaneous prostate biopsy to general urological surgeries is a safe and feasible approach. The transperineal approach has a lower incidence of complications. This method may benefit certain patients who are concurrently undergoing general urological surgeries and are under suspicion of prostate cancer in real-world clinical practice.

Correspondence to: Dr Qi Ma, Comprehensive Urogenital Cancer Center, Ningbo First Hospital, The Affiliated Hospital of Ningbo University, 59 Liuting Street, Ningbo, Zhejiang 315010, P.R. China
E-mail: qi.ma@nbdyyy.com

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Introduction

Prostate cancer (PCa) is the most common malignancy in males in developed countries (1). Its associated morbidity in Asian countries is also increasing rapidly (2). For the diagnosis of PCa, prostate biopsy is the gold standard, which is normally performed by transrectal or transperineal approach under ultrasound guidance (3). According to the current guidelines, a biopsy is performed under three indications: i) Abnormal digital rectal exam (DRE); ii) increased prostate-specific antigen (PSA); and iii) abnormal imaging (4).

Generally, prostate biopsy is a safe procedure. The Prostate Testing for Cancer and Treatment study observed that at 35 days after a biopsy was performed, the prevalence of minor complications is 92.6% for hematospermia, 65.8% for hematuria, 43.6% for pain, 36.8% for hematochezia and 17.5% for fever (5). Transient hematospermia and hematuria are the most frequent complications, which are usually self-limiting and will disappear in a few days or weeks without clinical intervention (6). There is a low risk of acute urinary retention and the majority of cases are resolved with transient placement of a urethral catheter and do not require any invasive treatment (7). Major complications include sepsis and severe rectal bleeding. Sepsis is the most dangerous complication of prostate biopsy and is potentially life-threatening; however, severe post-procedural infections are rare and have been reported in <1% of cases (8). The transperineal approach has been demonstrated to have a lower risk of infection compared with that of the transrectal approach (9). Major bleeding can occur in patients with coagulopathy and arterial injury and compression with a rectal balloon may help to arrest the bleeding. If bleeding persists, proctoscopy-guided clipping or cauterization are required (7).

Puncture-related pain is also a concern. It is recognized that transperineal biopsy requires anesthesia (10). Although the European Association of Urology (EAU) guidelines recommend local anesthesia for the transrectal biopsy (TRB) procedure (4), numerous hospitals in China do not administer anesthesia during TRB (11). Although it is well tolerated by multiple patients, the procedure can cause pain and discomfort. Severe pain can result in increasing patient movements or unwillingness to provide consent, which may lead to a decrease in diagnostic accuracy (12).

During clinical practice, certain patients who require urological surgery may occasionally be found to have abnormal PSA levels (>4 ng/ml) or to exhibit abnormalities on imaging such as magnetic resonance imaging (MRI) and/or ultrasound during preoperative examination. In the majority of cases, patients are advised to accept biopsy prior to surgery. Following biopsy and a definite pathology result, new medical decisions would be made based on the result of pathology (4). However, in the real world, this procedure involves a prolonged hospital stay, increased expense and elevated physical and psychological burden for certain patients. Additionally, a number of patients are averse to the pain associated with biopsy and prefer to receive both biopsy and surgery simultaneously under anesthesia (13). Therefore, patients are carefully selected to receive simultaneous biopsy and surgery under the same type of anesthesia during clinical practice.

The present retrospective study aimed to assess the feasibilities and outcomes of patients treated with simultaneous prostate biopsy and general urological surgeries. As the present study belonged to a series of studies performed in our Comprehensive Urogenital Cancer Center, the present study was named YH-prostate-001.

Materials and methods

Patient inclusion and exclusion criteria. The medical records of 49 male patients aged 56 to 91 years old who underwent prostate biopsy and urological surgeries simultaneously from October 2016 to June 2019 at Ningbo First Hospital (Ningbo, China) were retrospectively reviewed. The inclusion criteria were: i) Abnormal DRE and/or elevated serum PSA (>4 ng/ml) and/or imaging abnormalities during hospitalization; ii) no contraindications to prostate biopsy or urological surgeries; and iii) patients were suggested to accept simultaneous prostate biopsy and urological surgeries after being carefully informed of the possible complications. The exclusion criteria were: i) Patients had severe comorbidities and could not tolerate prostate biopsy and surgery; and ii) patients refused to accept simultaneous prostate biopsy and surgery. The enrolled patients clearly knew that it was not a standard procedure. Written informed consent was obtained from each patient.

Biopsy procedures. Among the 49 cases, 29 underwent preoperative multi-parameter magnetic resonance imaging (mpMRI) to obtain the patients' prostate imaging report and data system (PI-RADS) scores (14). Patients with a PI-RADS score of ≤3 received cognitive fusion targeted combined with systematic biopsy, while the remaining patients received systematic biopsy.

Prostate biopsy was performed in an operation room using an 18-gauge biopsy needle. After spinal or general anesthesia, the biopsy was carried out by a physician (RS) who had >5 years of experience and was familiar with cognitive fusion targeted biopsy and systemic biopsy. The biopsy was guided by a 7.5 MHz endocavity ultrasonic probe with MyLab40 (Esaote S.p.A.) or HI-VISION Preirus (Hitachi, Ltd.) ultrasound system. Biopsies were initially performed using the transrectal approach but were conducted via transperineal approach after September 2018, when the new equipment (HI-VISION Preirus) was purchased.

Simultaneous urological surgeries performed in the cohort. The types of urological surgeries performed in the present cohort included transurethral prostatectomy (TURP), ureteroscopic lithotripsy (URSL), laparoscopic renal cyst decortication (LRCD), cystostomy and ureteral stent extraction (USE). All the TURP and cystostomy cases had catheter indwelling before surgery, while the others had no catheterization. The TURP cases were limited to patients with prostatic hyperplasia complicated by acute urinary retention (AUR), who were suspected to have cancer but were considered to be unsuitable for local definitive treatment such as radical prostatectomy due to decreasing life expectancy or severe comorbidities. In addition, after being informed, certain patients refused potentially aggressive cancer treatments such as radiotherapy or brachytherapy, and these patients were also included in the present study.

Every case received routine urine examination. Preoperative urine culture was performed for urinary tract infection cases and targeted antibiotic therapy was administered if the result was positive. Other patients received prophylactic intravenous or oral antibiotics such as second-generation cephalosporins, quinolones or aminoglycosides from the day of operation, with a course of one to three days. Notably, after anesthesia, TURP patients were biopsied preoperatively, while the other patients were biopsied postoperatively.

Follow-up. All patients were interviewed by either a clinic nurse or a physician to assess possible complications. Patient information was evaluated retrospectively, including age, PSA level, PI-RADS score, pathological results and complications within 3 days, 1 month and 6 months after biopsy. The detection of clinically significant PCa (csPCa) was recorded. csPCa was defined as Gleason score of 3+4 or higher (ISUP >2).

Since the majority of the simultaneous operations were TURP, 50 cases of TURP treated by routine procedures in the same period were collected and the waiting time for TURP (from first admission to receiving TURP), length of hospital stay, hospitalization cost and postoperative complications between the simultaneous group (group one) and the routine procedure group (group two) were compared. The routine procedure at Ningbo First Hospital refers to the patient being discharged after receiving prostate biopsy at the first admission. If the pathological results were confirmed to be benign after seven to ten days, the patient would be readmitted for TURP.

Statistical analysis. All data were analyzed using SPSS version 20.0 software (IBM Corp.). First, Shapiro-Wilk test was used for normality test. Normally distributed variables

Table I. Patient characteristics of each surgical type.

Surgical type	Cases (n)	Case No.	Age (year), median (range)	PSA (ng/ml), median (range)	Prostate volume (ml), median (range)
TURP	41	-	80 (75-91)	9.1 (1.5-88.0)	56 (43-95)
URSL	2	1	56	12.3	36
		2	72	12.0	52
LRCD	2	1	70	6.8	33
		2	72	4.1	69
Cystostomy	2	1	73	158	32
		2	77	8.8	45
USE	2	1	68	6.8	38
		2	73	2.7	35

PSA, prostate specific antigen; TURP, transurethral resection of prostate; URSL, ureteroscopic lithotripsy; LRCD, laparoscopic renal cyst decortication; USE, ureteral stent extraction.

were presented as mean ± standard deviation and were compared between groups using unpaired Student's t-test. Non-parametric data were presented as the median (range) and were compared between groups using Mann-Whitney U test. Categorical variables were presented as number or number (percentage) and were analyzed via Fisher's exact test or the Continuity Correction Chi-squared test. $P<0.05$ was considered to indicate a statistically significant difference.

Results

Patients' characteristics and types of simultaneous urological surgeries. The patients' characteristics of each surgical type are listed in Table I. Of the 49 biopsy cases, 41 patients were treated by TURP, two by URSL, two by LRCD, two by cystostomy and two by USE.

PCa detection during simultaneous urological surgeries. A total of 41 patients received preoperative biopsy, while eight patients received postoperative biopsy. In total, 36 biopsies were transrectal and 13 biopsies were transperineal. A median of 10 biopsy cores (range, 6-12) were obtained, which included two target cores for patients with PI-RADS score of ≤3. The overall detection rate of csPCa was 22.4% (11/49), accounting for 91.7% (11/12) of all PCa cases. The detection of PCa by biopsy and simultaneous urological surgeries is shown in Table II. Furthermore, the results of biopsy and TURP in patients with prostatic hyperplasia complicated by AUR were analyzed individually and are listed in Table III. PCa was detected by biopsy alone in two cases, by both biopsy and TURP in three cases and by TURP alone in two cases. The positive rate of TURP and biopsy were both 12.2% (5/41), and there was no significant difference (Table III). In addition, the pathological results were compared according to different PI-RADS scores for patients who received mpMRI examinations. The detection rate of csPCa in patients with a PI-RADS score of 4-5 was 100%, while the rate in cases with PI-RADS score <3 was 7.1% (1/14). In TURP group, there was no PI-RADS 4 or 5 patients, and six cases were revealed to have csPCa. The association between PI-RADS score and pathological results of all cases and TURP patients is shown in Tables IV and V.

Table II. Prostate biopsy data and pathological results.

Variables	Value
Biopsy cores (n), median (range)	10 (6-12)
Biopsy sequence (n)	
Preoperative	41
Postoperative	8
Biopsy approach (n)	
Transrectal	36
Transperineal	13
Pathological results	
Overall (n)	
PCa	12
csPCa	11
Non-csPCa	1
Benign	37
Biopsy pathology (n)	
PCa	10
csPCa	9
Non-csPCa	1
Benign	39

PCa, prostate cancer; csPCa, clinically significant PCa.

Postoperative complications. Postoperative complications that occurred within 3 days included hematuria in 39 (79.6%) cases, fever in three (6.1%) cases and hematochezia in two (4.1%) cases. Fever occurred 1 day post-surgery and the highest temperature recorded was 38˚C. None of the three patients with fever had important co-morbidities or voiding symptoms. The results of urinalysis, urine and blood culture were negative and the fever subsided after physical hypothermy. There was no significant difference in the incidence of hematuria between

Table III. Prostate biopsy results among patients who underwent TURP.

	Biopsy pathology (n)		
TURP pathology	PCa	Benign	Total (%)
PCa	3	2	5 (12.2)
Benign	2	34	36 (87.8)
Total (%)	5 (12.2)	36 (87.8)	41 (100)

PCa, prostate cancer; TURP, transurethral resection of prostate.

Table IV. Correlation between MRI and csPCa.

PI-RADS score	Cases (n)	csPCa (n)	Detection rate (%)
<3	14	1	7.1
3	12	3	25
4	2	2	100
5	1	1	100
Not available	20	4	20
Total	49	11	22.4

PI-RADS, prostate imaging reporting and data system; csPCa, clinically significant prostate cancer.

the transrectal and transperineal approaches (86.1 vs. 61.5%; P=0.104). However, the overall incidence of complications was significantly reduced after switching from transrectal to transperineal approach (97.2 vs. 69.2%; P=0.014). No complications were observed 1 or 6 months post-surgery (Table VI).

Comparison of simultaneous and routine procedure in TURP patients. Further analysis was performed between simultaneous and routine procedure groups of TURP cases. The waiting time for TURP, hospital stay length and hospitalization cost of group one were significantly lower compared with those of group two (P<0.05). The two groups did not exhibit significant differences in postoperative hematuria duration, fever or temporary incontinence (Table VII).

Discussion

In standard practice, a prostate biopsy is an independent procedure and has been demonstrated to be a safe and effective method for the diagnosis of PCa (6,15). However, few studies have focused on the safety and feasibility of simultaneous prostate biopsy and urological surgeries. Several studies have discussed the possibility of simultaneous biopsy and TURP for patients with AUR. Yang *et al* (16) reported a total of 34 patients with AUR and elevated PSA (>4 ng/ml) who underwent concomitant transrectal biopsy and TURP. Complications include fever in five cases (14.7%), re-catheterization for urine retention in two cases (5.9%), urinary tract infection in two cases (5.9%) and urge incontinence in

Table V. PI-RADS score and pathological results of patients who underwent TURP.

PI-RADS score	Cases (n)	PCa (n)	csPCa (n)
<3	13	3	2
3	9	3	3
>3	0	0	0
Not available	19	1	1
Total	41	7	6

PI-RADS, prostate imaging reporting and data system; PCa, prostate cancer; csPCa, clinically significant PCa; TURP, transurethral resection of prostate.

Table VI. Statistics of postoperative complications.

	Biopsy approach			
Complications	Transrectal	Transperineal	P-value	Total
Total patients	36	13	-	49
Patients with complications	35 (97.2%)	9 (69.2%)	0.014[a]	44
Within 3 days				
Hematuria	31 (86.1%)[b]	8 (61.5%)[c]	0.104	39
Fever	2 (5.6%)[d]	1 (7.7%)[e]	-	3
Hematochezia	2 (5.6%)[d]	0	-	2
1 month	None	None	-	None
6 month	None	None	-	None

Data are presented as n, n (%). [a]P<0.05 is statistically significant. [b]30 TURP, one URSL; [c]four TURP, one URSL, two Cytostomy, one USE; [d]two TURP; [e]one LRCD. TURP, transurethral resection of prostate; URS, ureteroscopic lithotripsy; USE, ureteral stent extraction; LRCD, laparoscopic renal cyst decortication.

seven cases (20.6%). It was revealed that, compared with the 40 patients with AUR who underwent TURP alone, the rate of complications does not significantly increase. Cho *et al* (13) reported that combined transrectal prostate needle biopsy and TURP is safe, as no notable complications are observed other than fever. Another study on 42 AUR cases also demonstrated that simultaneous biopsy and TURP does not increase the risk of morbidity (17). Furthermore, with this approach, patients can recover from the stress of urinary retention and have a definite diagnosis (17).

The present study expanded on the types of general urological surgeries performed at the same time as biopsy and used two biopsy approaches successively. To the best of our knowledge, this type of preliminary study has not been reported to date. The results revealed that only mild postoperative complications were observed with both approaches. Hematuria was the most common complication, which was caused by biopsy and was also associated with the operation. TURP, URSL, USE may also cause postoperative hematuria. However, such hematuria is usually self-limiting and does

Table VII. Comparison of simultaneous and routine procedure in TURP patients.

Variables	Group 1 (n=41)	Group 2 (n=50)	P-value
Age, years[a]	80 (75-91)	73 (56-86)	<0.001[b]
PSA, ng/ml[a]	9.1 (1.5-88.0)	8.0 (4.0-75.2)	0.67
Prostate volume, ml[a]	56 (43-95)	56 (36-82)	0.55
Waiting time for TURP, days[c]	2.9±0.7	11.7±1.6	<0.001[b]
Hospital stay length, days[c]	10.9±2.3	12.4±2.3	<0.001[b]
Hospitalization cost, CNY[c]	14,093.5±1,902.5	15,097.0±2,354.0	0.03[b]
Postoperative hematuria duration, days[c]	9.6±2.7	9.4±2.2	0.82
Fever, n	2	3	1.00
Temporary incontinence, n	3	2	0.82

[a]median (range). [b]P<0.05 was considered to indicate statistical significance. [c]mean ± SD. PSA, prostate specific antigen; TURP, transurethral resection of prostate; CNY, Chinese yuan.

not require medical intervention. The patients who had fever did not have any other symptoms and their laboratory results were negative; therefore, they were considered to have a non-infectious reactive fever. Hematochezia usually occurs in transrectal biopsies, but rarely occurs in transperineal biopsies; thus, it is also self-limiting (6). The present study compared the transrectal approach with the transperineal approach and the incidences of hematuria were equal, while the overall rate of complications were significantly lower in the transperineal approach compared with the transrectal approach. A recent meta-analysis study indicated that both transperineal and transrectal prostate biopsy approaches have the same diagnostic accuracy, but the transperineal approach has a lower risk of fever and rectal bleeding compared with the transrectal approach (18). These results suggest that the transperineal approach may be the safer option when biopsy and surgery are performed simultaneously. However, due to the small sample size, additional studies are needed to further verify this conclusion.

TURP is rarely used as a tool for the diagnosis of PCa. Before the application of mpMRI, TURP has only been used in selected cases to rule out PCa in males with a suspicion of PCa despite a negative prostate biopsy (19). However, TURP can only detect tumors in the transition zone of prostate, only accounting for 15-30% of cancer cases (20). Therefore, in addition to TURP, it is also necessary to apply biopsy to patients with both AUR and high PSA values. In the present study, the positive rates of TURP and biopsy were similar and complementary to each other. The total detection rate among these patients was only 12.2% (5/41) and it was possibly caused by PSA false positives in numerous AUR cases.

mpMRI has been recommended by the EAU guidelines since 2019 to improve the detection accuracy of csPCa (4,21). However, in the present cohort, mpMRI was not performed in all cases. From the available data, the detection rate of csPCa in patients with a PI-RADS score of 4-5 was 100%, while in patients with PI-RADS score <3 the rate was only 7.1%, which suggested that mpMRI may be useful for the prediction and screening of high-risk cases, as mentioned in previous studies (21,22). A recent study suggested that a greater number of prostate biopsy cores should be obtained in patients who did not receive preoperative mpMRI scan (23). However, as the current study enrolled patients during 2016 to 2019, biopsy cores were not improved during that period.

Since the main surgery type was TURP, the present study further compared the simultaneous group and the routine procedure group of patients, who received biopsy before TURP. It demonstrated that the waiting time for TURP, hospital stay length and hospitalization cost were significantly lower in simultaneous group, while the complications were equal. This indicated that simultaneous biopsy and TURP had certain advantages over traditional methods. However, there is a potential disadvantage of simultaneous prostate biopsy and TURP that affects patients with PCa who are suitable candidates for radical prostatectomy or other definitive local therapies such as radiotherapy or brachytherapy. Previous studies have shown that patients with a history of TURP have a poorer prognosis after laparoscopic radical prostatectomy (24,25). It is also more difficult for surgeons to perform a robot-assisted radical prostatectomy on patients with a history of TURP (26). Therefore, strict enrollment criteria were applied for TURP patients in the current study. All the selected cases were deemed unsuitable for local treatment due to decreased life expectancy (>80 years old) or severe comorbidities such as cardiac disorder, malignancy or patients' refusal to receive any aggressive procedures such as radiotherapy or brachytherapy. For other urological surgeries, no side effects associated with concomitant biopsy were observed.

The current preliminary study showed that the approach of simultaneous prostate biopsy and general urological surgeries was safe and feasible. It was concluded that this method has several advantages. Firstly, intraoperative anesthesia can control pain and relax rectum muscles, which ensures the accuracy and ease of biopsy. Furthermore, the pain or discomfort experienced by the patients can be avoided. Secondly, it can reduce the length of hospital stay, expenses and psychological burden for certain patients. Thirdly, doctors' working efficiency can be improved without increasing complications.

The present study also had several limitations: i) It included a small sample size and only certain types of general urological surgeries were involved; and ii) it was a retrospective study so

it was difficult to include a suitable control group. Therefore, only results from previous studies could be compared and it was found that there was no significant increase in the risk of complications (15-17,27). Despite these limitations, advantages of simultaneous prostate biopsy and general urological surgeries were observed, which suggested that this method may help real-world patients who concurrently undergo general urological surgeries and suspicion of PCa.

In conclusion, according to the present findings, combining simultaneous prostate biopsy and general urological surgery is a safe and feasible approach. Transperineal approach was observed to have a lower incidence of complications. However, as an unconventional procedure, it should be emphasized that patients with PCa diagnosed by TURP and simultaneous prostate biopsy may negatively affect local definitive treatment such as radical prostatectomy. Therefore, it is important to note that this procedure is recommended only for carefully selected cases and patients should be fully informed before providing consent.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Authors' contributions

RS, QM and JHJ designed the study. RS performed the prostate biopsies. RS and QM prepared the manuscript. JFP and CLY participated in the collection and analysis of data and statistics. RDH and ZLT conducted patient follow-up and partial data collection. All authors have contributed to, read and approved the final manuscript. QM and RS confirm the authenticity of all the raw data.

Ethics approval and consent to participate

The patients/participants provided their written informed consent to participate in this study. As only routine clinical practices were involved in this study and patients' data were retrospectively collected and analyzed, only submitted materials were reviewed and approved by the ethical review committee of Ningbo First Hospital (approval no. 2021-R084).

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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