Needle Tip Culture after Prostate Biopsy: A Tool for Early Detection for Antibiotics Selection in Cases of Post-Biopsy Infection

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Purpose: To investigate biopsy needle tip culture after prostate biopsies for bacteria prediction and antibiotics selection.

Materials and Methods: From May 2017 to April 2019, 121 patients who underwent a prostate biopsy were enrolled. All biopsy needle tips were sent for aerobic and anaerobic culture. Patients were divided into positive and negative culture groups. Perioperative data were recorded and compared between the two groups. The culture time and susceptibility of febrile patients were analyzed. Blood cultures were conducted for all patients who experienced fever after biopsy. The time and results of the needle and blood cultures were recoded for descriptive analysis.

Results: There were 59 (48.8%) positive needle cultures. Other than fever (p = 0.023), there were no statistical significances in clinical data between the two groups. Fever occurred in eight patients, and seven febrile patients had positive needle cultures, six of whom had positive blood cultures. These six needle and blood cultures were consistent with the susceptibility test results. As compared to the waiting time for blood cultures, target antibiotics were administered at an average of 48.0 h earlier based on needle cultures. None of the patients with positive anaerobic cultures developed a fever, while all eight febrile patients had negative anaerobic cultures.

Conclusion: Fevers developed at statistically significant higher rate among those who had positive needle cultures. Needle and blood cultures were consistent with the susceptibility test results. Needle cultures can help us administer target antibiotics earlier to febrile patients without the need to wait for blood cultures.

Keywords: biopsy; needle; culture; anti-bacterial agents; prostatic neoplasms

INTRODUCTION

Prostate cancer was the second most common cause of cancer-related death among men in the United States in 2018.[1] Transrectal ultrasound-guided prostate biopsy (TRUSPB) is the gold standard for the diagnosis of prostate cancer.[2] Regardless of whether the objective is diagnosis or active surveillance of prostate cancer, or whether the method involves systematic sextant biopsy or a combined method of magnetic resonance imaging with ultrasound fusion-guided targeted biopsy, with any transrectal procedure, infection remains a common complication.

Despite the prescription of antibiotic prophylaxis, the infection rate after TRUSPB is reportedly 0%–6.3% and can potentially progress to sepsis.[2,3] Although sepsis-related mortality is relatively rare, with an incidence of 0.095%–0.24%,[4, 5] mortality and the development of sepsis after TRUSPB are disastrous. According to the Surveillance of Multicenter Antimicrobial Resistance in Taiwan in 2018, the ciprofloxacin resistance rate of E.coli was about 31.2%, and this associated with risk of infection.[6] As for high risk patients, such as those with diabetes mellitus and geriatric patients,[7-9] physicians concerned with severe complications may delay prostate biopsy procedures. Hence, it is important to find an antibiotics selection detection tool.

Because infection may lead to sepsis or even mortality, post TRUSPB infection-related issues are concerning; thus, management is needed to prevent such complications both before and after a biopsy.[10-12] More specifically, the prediction of pathogenic bacteria and the choice of an appropriate antimicrobial agent are the most important considerations. Although blood culture (B/C) and rectal swab cultures are advocated, the former is time-consuming and the latter is used for prevention, not post-biopsy infection management, as it is focused on prophylaxis and the prediction of antimicrobial resistance preoperatively, rather than the management of post TRUSPB infection of febrile patients.

Pathogens in the rectal mucosa can be inoculated in the prostate and blood stream by the biopsy needle, thereby inducing infection.[13] Typically discarded as medical waste, the biopsy needle is the first instrument to come in contact with pathogens, thus it is relatively simple to culture pathogens attached to the needle that induce fever after TRUSPB in real-time.

Tip cultures of intravenous lines, suction tubes, and

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Table 1. Stratification of variable of interest for patients with positive (n = 59) and negative (n = 62) biopsy needle culture results

	Positive	Negative	*P* value
Demographic variables			
Patients, n	59	62	
Age, years			
Mean ± SD	66.55 ± 8.60	66.92 ± 8.64	0.813
Prostate volume (mL)			
Mean ± SD	55.91 ± 28.59	54.37 ± 21.97	0.767
PSA (ng/mL)			
Median (25th–75th percentile)	14.1 (7.12–35.96)	12.85 (7.89–49.88)	0.620
Pre-OP WBC (×103/uL)			
Mean ± SD	7.51 ± 2.18	6.77 ± 2.32	0.129
Pre-OP Cr (mg/dL)			
Mean ± SD	0.97 ± 0.30	0.94 ± 0.35	0.652
Pre-OP sugar (g/dL)			
Mean ± SD	123.67 ± 43.89	118.51 ± 40.83	0.576
Pre-OP GOT (U/L)			
Mean ± SD	23.40 ± 7.47	28.59 ± 13.78	0.057
Pre-OP GPT (U/L)			
Mean ± SD	20.82 ± 7.77	27.59 ± 22.25	0.057
Pre-OP PT (s)			
Mean ± SD	11.04 ± 0.80	11.10 ± 0.95	0.759
Pre-OP APTT (s)			
Mean ± SD	33.51 ± 4.06	34.05 ± 3.68	0.528
Pre-OP Urine culture (n)			0.485
Positive	7	5	
Negative	52	57	
Pathology (n)			
Benign	34	28	0.170
Malignant	25	34	
Fever (n)			0.023[a]
Fever	7	1	
No fever	52	61	
CPPS (n)	0.588		
Yes	1	2	
No	58	60	
Diabetes mellitus (n)	0.138		
Yes	10	5	
No	49	57	
Hypertension (n)			0.716
Yes	12	11	
No	47	51	
Rectal disease (n)			0.818
Yes	5	6	
No	54	56	

[a]$p < 0.05$.
Pre-OP = preoperative; WBC = white blood cell; Cr = creatinine; GOT = glutamic oxaloacetic transaminase; GPT = glutamic pyruvic transaminase; PT = prothrombin time; APTT = activated partial thromboplastin time; CPPS = chronic pelvic pain syndrome.

chest tubes have been investigated as predictors of infection and even bacteremia in previous studies.[14-16] Furthermore, Peacock et al. reported that 23.5% of positive intravenous line tip cultures were associated with B/C positivity for the same microbial species with matching susceptibility test results.[14] Unlike investigations of other tip cultures, the use of a biopsy needle tip culture (N/C) after TRUSPB has not been reported, which peaked our interest in N/C studies of febrile patients after TRUSPB. In order to investigate whether N/C can predict pathogens and help to choose an appropriate antimicrobial agent, we evaluated the clinical data on TRUSPB cases over a 2 year period at our hospital.

MATERIALS AND METHODS

The Institutional Review Board of Chiayi Christian Hospital approved the study protocol (Chiayi, Taiwan; approval no. 2018079). The study cohort was limited to patients who underwent TRUSPB at Chiayi Christian Hospital from May 2017 to April 2019 and men with either an increased concentration of prostate-specific antigen (PSA) (ng/mL) and/or suspicious digital rectal examination results. Patient histories of perineal pain, chronic pelvic pain syndrome, previous TRUSPB, rectal-related disease, prostate volumes, and abnormal prostate findings by transrectal ultrasound were recorded. Routine blood analysis as well as urinalysis and urine culture (U/C) were checked preoperatively. Antibiotic prophylaxis with fluoroquinolone was administered for a total of three days (preoperative day 1, the day of surgery, and postoperative day 1).

BARD® MAX-CORE® Disposable Core Biopsy Instruments (C.R. Bard, Murray Hill, NJ, USA) were used for all biopsies. The biopsy needle tips were cut off with sterile wire cutters, 4–5 cm in length, for aerobic and anaerobic cultures. B/Cs of febrile patients were conducted upon return to our hospital. Patient characteristics, blood/urine analysis, number of biopsy cores, postoperative complications, B/C, and N/C results were recorded for analysis. The saving time was also recorded by calculating from the time of prescribing target antibiotics based on N/C results to the time of obtaining the B/C results of febrile patients.

Table 2. Description of biopsy needle tip cultures and blood cultures of febrile patients

	Case 8		Case 15		Case 18		Case 49		Case 93		Case 118		Case 120		Case 121	
	N/Ca	B/Cb	N/C	B/C	N/C	B/C	N/C	B/C	N/C	B/C	N/C	B/C	N/C	B/C	N/C	B/C
Bacteria	E.coli	E.coli	E.coli	E.coli	E.coli	-	E.coli	E.coli	E.coli	E.coli	E.coli	E.coli	E.coli	E.coli	-	-
Susceptibility test																
Ampicillin/Sulbactam	Rd	R	S	S	S		S	S	S	S	S	S	R	R		
Piperacillin/Tazobactam	Se	S	S	S	S		S	S	S	S	S	S	S	S		
Gentamicin	S	S	S	S	S		R	R	S	S	R	R	R	R		
Amikacin	S	S	S	S	S		S	S	S	S	S	S	S	S		
Levofloxacin	R	R	R	R	R		R	R	R	R	R	R	R	R		
Ertapenem	S	S	S	S	S		S	S	S	S	S	S	S	S		
Meropenem	S	S	S	S	S		S	S	S	S	S	S	S	S		
Trimethoprim/Sulfamethoxazole	R	R	R	R	R		R	R	R	R	R	R	R	R		
Cefazolin	R	R	R	R	R		S	S	R	R	I	I	R	R		
Cefuroxime	If	R	R	R	R		S	S	R	R	S	S	R	R		
Cefotaxime	R	R	R	R	R		S	S	R	S	I	I	R	R		
Cefepime	S	S	Dg	D	D		S	S	D	S	S	S	R	R		
Saving timec (h) Mean 48.0 h	25		73	-			43		26		62		59		-	

aBiopsy needle tip culture. bBlood culture. cSaving time: saving the waiting time for blood culture the time from prescribing antibiotics based on susceptibility tests of T/C to getting results of B/C. dResistant. eSusceptible. fIntermediate. gSusceptible-dose dependent.

Descriptive and comparative analyzes were performed using IBM SPSS Statistics software, version 21.0 (IBM Corp., Armonk, NY, USA). Three types of statistical analyzes were used (i.e., an independent-sample t-test, Mann–Whitney U test, and chi-squared test) to identify differences in variables between patient groups with positive vs. negative N/C results. A probability (p) value of < 0.05 was considered statistically significant.

RESULTS

In total, 121 consecutive patients (mean age, 66.7 ± 8.62 years) underwent TRUSPB in our hospital during the study period. The mean prostate volume was 55.1 ± 25.46 mL and the median prostate-specific antigen (PSA) was 13.5 (25th–75th percentile, 7.54–42.92) ng/mL. Preoperative U/C results were positive in twelve patients. Eight patients (6.6%) developed fever after TRUSPB and the mean time to fever onset after the biopsy in the study period was 51.57 ± 36.05 hours.

Biopsy needle cultures were positive in 59 (48.8%) of 121 patients. The patients were assigned to the N/C-positive or -negative group. As shown in Table 1, there were no significant differences between two groups in age, prostate volume, PSA level, preoperative laboratory tests, and U/C results. There was also no significant difference in the pathology results and underline diseases. The postoperative fever was the only variable with a significant difference ($p = 0.023$) between the two groups.

Furthermore, we recorded the B/C and N/C results of the febrile patients; seven of eight febrile patients with N/C results were positive for Escherichia coli (*E*. coli). As shown in Table 2, the B/C results of six patients were also positive for *E*. coli. All of the pathogens detected by N/C and B/C were resistant to fluoroquinolone and notably, they were susceptible to piperacillin/tazobactam, amikacin, and carbapenem. Furthermore, the N/C and B/C results were consistent with the findings of the susceptibility tests.

The culture times of all positive N/Cs are shown in Figure 1A and the times to obtain the N/C and B/C results of febrile patients are shown in Figure 1B. Of the 121 patients, the N/C results were positive in 59 (48.8%), which included 54 positive aerobic cultures and nine positive anaerobic cultures. Among the 59 positive N/Cs, only four cases had positive results for both aerobic and anaerobic bacteria. Seven of eight febrile patients had positive N/C results, including six positive and two were negative for B/C (**Figure 1B**). The saving times were 25, 73, 43, 26, 62, and 59 h in cases 8, 15, 49, 93, 118, and 120, respectively. The mean saving time was 48.0 h.

In case 49 of Figure 1B, the N/C results were obtained before the onset of fever and returning to the hospital; the mean time to receiving the B/C results was 43.0 h. Upon receiving a positive N/C result, the patient was administered the target therapeutic antimicrobial agent based on N/C in the emergency room. The saving time was 43.0 h.

Of the positive N/C samples (n = 59), the most common bacterium was E. coli (n = 34, 57.6%), which was identified in seven of eight febrile patients and 27 of 62 afebrile patients. Nine patients had positive anaerobic N/C results, but none developed a fever. Details of the detected bacteria are listed in **Table 3**.

DISCUSSION

In the present study, the N/C results were positive for 59 (48.8%) patients. The most common bacterium was E. coli (57.6%). Fever developed in eight patients. Seven of them had positive N/C and all the results were E. coli and six of the seven N/C results were consistent with the B/C findings. The average saving time was 48.0 h (**Figure 1B**). Of the nine patients with positive anaerobic cultures, none developed a fever and none of the four febrile patients had positive anaerobic cultures. In general, the prediction of pathogenic bacteria and the early administration of target antibiotics were based on the B/C and U/C results. B/C is the gold standard and first-line test for blood stream infections,[17] but it is time-consuming and does not always yield positive results for febrile patients. Although many new methods and automated B/C systems for the diagnosis of positive B/Cs with reduction of culture time are available,[18] the indication for B/C was that bacteremia was suspected, such as fever or leukocytosis;[19] therefore, the timing of collecting B/Cs was later than that of N/Cs; thus, B/C results might be obtained later. Because the biopsy needle is the first real time object to come into contact with potential pathogens, N/C was performed

Table 3. Aerobic and anaerobic bacteria of febrile and afebrile patients

	Non-Fever	Fever
Aerobic (patient number,%)	47(38.8%)	7(5.8%)
Escherichia coli	27	7
Enterococcus faecalis 7		
Streptococcus mitis/oralis (viridans group)	5	
Klebsiella pneumoniae	5	
Streptococcus group B4		
Streptococcus anginosus (viridans group)	3	
Bacillus spp.	2	
Acinetobacter baumannii	2	
Enterococcus hirae	1	
Enterococcus raffinosus	1	
Enterococcus faecium 1		
Enterobacter agglomerans	1	
Streptococcus pasteurianus (S. bovis biotype II.2)	1	
Streptococcus alactolyticus (viridans group)	1	
Brevundimonas diminuta/vesicularis 1		
Streptococcus anginosus (viridans group)	1	
Streptococcus salivarius	1	
Sphingomonas paucimobilis	1	
Granulicatella adiacens	1	
Anaerobic (patient number,%)	9(7.4%)	0(0%)
Bacteroides fragilis	3	
Clostridium perfringens	1	
Bacteroides thetaiotaomicron	1	
Bifidobacterium spp	1	
Fusobacterium nucleatum	1	
Parabacteroides distasonis	1	
Peptostreptococcus anaerobius	1	

immediately after the biopsy. Therefore, the N/C results were obtained earlier than those of B/C for the timely diagnosis of fever when patients presented to the hospital. In the cohort of the present study, there were six febrile patients with positive results for both B/C and N/C. Notably, the B/C and N/C results of each patient were consistent with the findings of the susceptibility tests. In the previous use of target antibiotics, we often waited for the susceptibility test results of B/C.[12] If the N/C and B/C results are in agreement with those of the susceptibility tests, time can be saved waiting for B/C results, as it is possible to prescribe target antibiotics for pathogens based on the N/C results alone. In this study, we did not have to wait for B/C, and we were able to save an average time period of 48.0 h to identify a target antimicrobial agent based on N/C results, which was truly clinically beneficial (**Figure 1B, Table 2**).

In regard to pathogen prediction, the B/C results are not always positive in febrile patients. The reported B/C positivity rate of febrile patients after TRUSPB ranges widely from 16% to 78%.[20-22] In this study, six of eight febrile patients (75%) had positive B/C results, which is consistent with previous reports. Two febrile patients (case 18 and 121, 25%) had negative B/C results; thus, the susceptibility test of N/C was useful for selection of an appropriate antimicrobial agent. Because the N/C and B/C results were mostly consistent, if the B/C result was negative, N/C becomes the most important reference to select target antibiotics (**Table 2**).

U/C was also considered for the prediction of potential pathogens. However, as noted in previous studies, pathogens pre-existed in the rectum rather than the urinary tract, thus dysuria or a history of urinary tract infection was not predictive of a TRUSPB-related infection.[20] Therefore, preoperative U/C is less useful for the identification of pathogens after TRUSPB. This was revealed in the present study showing that only seven patients had positive preoperative U/C results, demonstrating no significance with the onset of fever.

Other than B/C and U/C, cultures of rectal swabs was recommended for the prediction of pathogens.[23] Because prophylaxis with fluoroquinolone is recommended by the guidelines of the American Urological Association and European Urological Association, rectal swabs were used to identify fluoroquinolone-resistant bacteria to facilitate target antibiotic prophylaxis in previous studies.[24] However, other investigations have revealed that this strategy does not reduce post TRUSPB-related infectious complications or hospitalization.[25,26] Therefore, using rectal swab cultures to prevent infection after TRUSPB remains controversial. Furthermore, rectal swab cultures focus on the prediction of antimicrobial resistance to direct appropriate administration of prophylactic antimicrobial agents. In addition, rectal swab cultures are usually conducted several days before a scheduled biopsy and, therefore, represent bacteria existing in the rectum several days beforehand, rather than real-time detection of pathogens that could induce fever after TRUSPB. Moreover, antimicrobial prophylaxis does not always prevent sepsis after transrectal prostate biopsy.[27,28]

At present, rectal swab cultures are not widely applied, as mentioned at the 2019 American Society of Clinical Oncology meeting in a report by Jonathan Shoag of the Surveillance, Epidemiology and End Results data.[29] In this study, of 246,299 males who underwent prostate biopsies, only 0.5% utilized pre-biopsy rectal swab procedures.

Another interesting point of discussion is the role of anaerobic bacteria in post TRUSPB infections. However, limited studies have mentioned anaerobic bacteria as potential pathogens of post TRUSPB infections.[30] In our study, prophylactic anti-anaerobic antimicrobial agents were not prescribed even though nine patients had positive N/C results for anaerobic bacteria (**Table 3**). Nonetheless, none of these nine patients developed

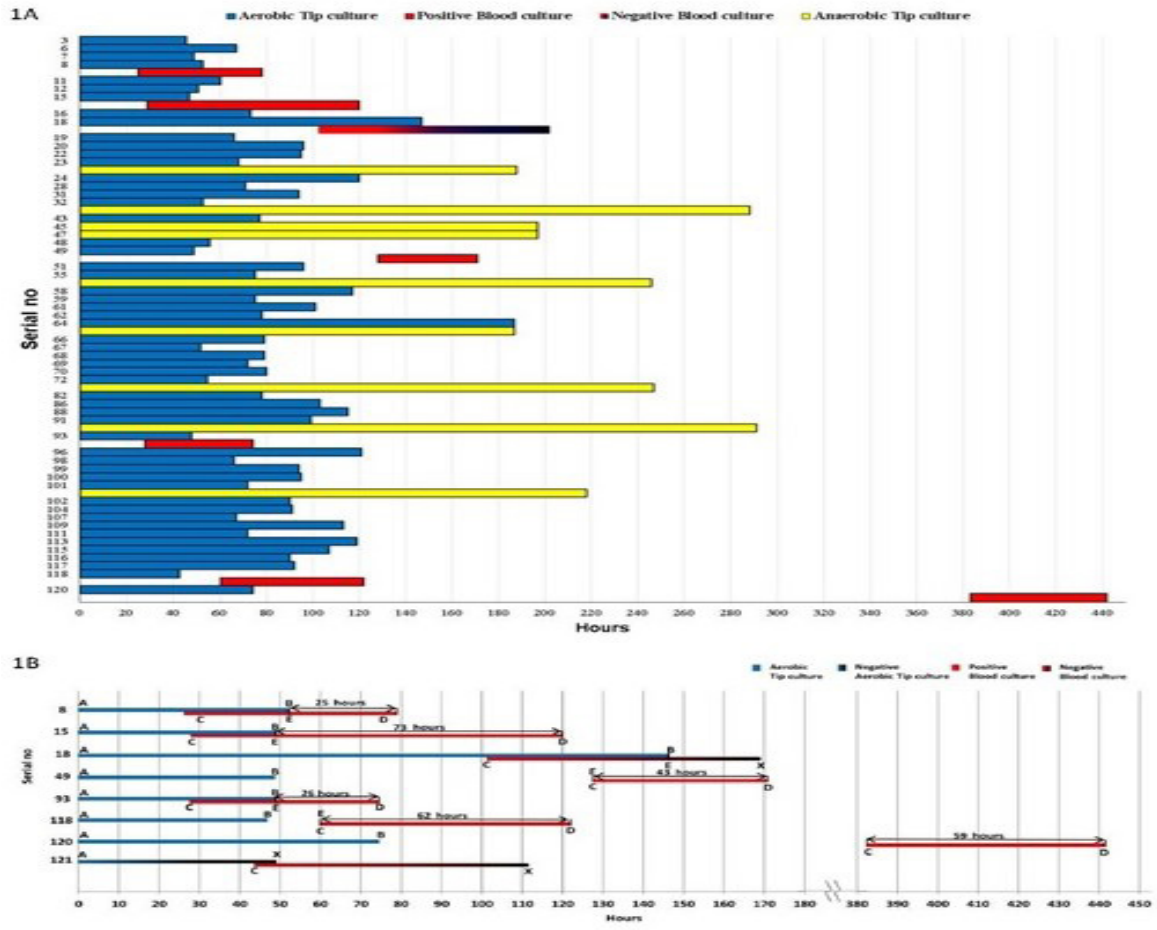

Figure 1. Time-consuming after procedure. Each number along the Y-axis represents a patient with a positive needle tip culture. Blue bars represent positive aerobic needle tip cultures, yellow bars represent positive anaerobic needle tip cultures, pure red bars represent positive blood cultures, and red-black bar represents negative blood cultures.
A. Calculation of the saving time in four febrile patients after biopsy. Each number along the Y-axis represents each febrile patient after biopsy. Blue bars represent positive aerobic needle tip cultures, pure red bars represent positive blood cultures, red-black bar represents negative blood cultures, and blue-black bar represents negative aerobic needle tip cultures. A: The days the needle tip cultures were performed. B: The times of obtaining results of needle tip cultures. C: The times the blood cultures of febrile patients were performed. D: The times the blood culture results were obtained. E: The times that antimicrobial agents were prescribed based on needle tip cultures. X: No growth in blood culture or needle tip culture. E to D: the saving time (48.0 h in average).

a fever and all febrile patients had negative N/C results for anaerobic bacteria. Therefore, we suppose that anaerobic bacteria are not regularly pathogens that induce fever after TRUSPB.

N/C is not expensive according to Taiwan National Health Insurance as each N/C costs about 6.3 US dollars. If considering cost effectiveness, we suggested that N/C can be applied in high risk geriatric, diabetes mellitus and immunosuppressed patients.

In addition to a reduction in hospital stay, the advantages of N/C are as follows: (1) allows for early use of target antimicrobial agents to prevent the clinical course progression to a more severe or irreversible condition; (2) B/C may be substituted by N/C when B/C is negative; (3) N/C can shorten the broad-spectrum antibiotic course to decrease the production of antimicrobial agents resistance; (4) early use of target antimicrobial agents can decrease the adverse effects of broad-spectrum antibiotics.

Limitations of the present study included the following: (1) the relatively low number of cases, which should be increased in future studies to increase the strength of evidence; (2) the rate of *E*. coli detection by N/C and B/C in febrile patients was consistent with that of the susceptibility test, although we did not identify the strains of these *E*. coli isolates. Thus sequencing of 16S rDNA is needed to arrive at a definitive confirmation; (3) we only calculated the saving time with the same culture procedure in our hospital, thus future studies of different cultural procedures are needed; and (4) postoperative U/C of febrile patients was not a focus of this study because of the delay in obtaining results; thus, further analyses are needed to determine if the collection of urine immediately after TRUSPB might have different results.

CONCLUSIONS

Fever was statistically significant in the N/C positive group. The N/C and B/C results were consistent with those of susceptibility testing. N/C can help to administer earlier targeted antibiotics to febrile patients, thus eliminating the need to wait for B/C results.

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