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Factors Predicting Complications Following Transrectal Ultrasound Guided Prostate Biopsy

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ABSTRACT *The aim of this study was to assess prospectively, the complications following transrectal ultrasound (TRUS) guided prostate biopsy and the risk factors for infection following the biopsy. A total of 89 patients under evaluation for suspected carcinoma prostate underwent a standard 12- core biopsy over a study period of one year. Data on 75 patients was evaluable. The mean age of patients was 60.69 years. Most common presentation was lower urinary tract symptoms. Diabetes and hypertension were the most common co-morbid illnesses. Only five patients developed fever post biopsy. One patient developed uro-sepsis and shock requiring hospitalisation. Subgroup analysis showed that presence of a positive urine culture was statistically associated with higher infection rates. The association with diabetes and indwelling catheter was not significant. TRUS guided prostate needle biopsy is safe for diagnosing prostate cancer. Treatment of infection and documentation of negative urine culture before biopsy is ideal.*

Introduction

The most common non-cutaneous cancer in United States is prostate cancer, an approximate 241,000 cases diagnosed in 2012 and also, the second most common cause of cancer-related death. Serum prostate-specific antigen (PSA) test and rectal examination are the currently recommended methods of screening for prostate cancer; however, the diagnosis can only be made after prostate needle biopsy.

Majority of the prostate biopsy related complications are mild and self-limited but sometimes it could be severe and life threatening requiring hospitalization. Multiple factors could be responsible, bacterial resistance and lack of standard antimicrobial prophylaxis before prostate biopsy is the most common factor.

This study was designed to assess the incidence and also the factors predicting complications following transrectal ultrasound (TRUS) guided prostate biopsy.

Material and methods

A prospective observational study was carried out at our institute from March 2014 to March 2015. Approval of Institutional Review Board and Ethics Committee was obtained.

Consecutive patients under evaluation for suspected carcinoma prostate were included in the study. All patients underwent detailed history and physical examination. Co-morbidities were assessed if any, especially diabetes mellitus. Anti-platelet drug like Clopidogrel was discontinued for atleast 7 days prior to biopsy.

Urine culture and sensitivity testing was done for all patients. If urine culture was negative, single dose of Inj. Amikacin 15mg/Kg IV was given just before doing biopsy. Positive culture was treated with appropriate antibiotics 3 days prior to biopsy and then continued for a total of 7 days. Peri-prostatic nerve block (PPNB) was given to all patients before TRUS guided prostate biopsy. Standard 12-Core prostate biopsy done in each patient and samples were and sent for pathology.

The primary outcome of the study was to assess the incidence of uro-sepsis following TRUS biopsy. The secondary outcomes were:

1) To assess the Incidence of other complications:

a. Infection – Any fever post biopsy more than 37.5 C°
b. Gross hematuria
c. Hematochezia
d. Urinary retention
e. Pain or discomfort

2) To find risk factors for occurrence of complications.

All patients' data including follow up, within 30 days of biopsy were prospectively recorded.

A target sample size of 75 was calculated. This was carried out assuming an average incidence of infection related complication of up to 6%. Statistical analysis was performed using Statistical Package for Social Sciences (SPSS®) version 18 (IBM Corporation, USA). Chi square test and Fisher's exact test were used to find the relationship between two variables.

Results

A total of 89 patients underwent TRUS guided prostate biopsy for suspected carcinoma prostate on the basis of raised PSA or abnormal rectal examination during study period. Fourteen patients were excluded from the study for lack of data. The remaining seventy five patients were included in the study.

The mean age of patients was 60.69 years. Diabetes and hypertension were the most common associated co-morbid illnesses, being seen in over 58% of the patients.

Table 1: Demographic characteristics (n= 75)

	Mean (standard deviation)
Age (yrs)	60.69 (9.57)
Prostate size (cc)	24.07 (13.29)
PSA (ng/ml)	96.75

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Co- morbidity	
DM	18
HT	26
CAD	01
COPD	02
Post CVA	02
CKD	01

Most common presentation of these patients was lower urinary tract symptoms (LUTS). During evaluation, they were suspected to have prostate cancer either by an abnormal rectal finding or raised PSA.

Among all the patients who underwent biopsy, only 38 (52%) patients were diagnosed as adenocarcinoma prostate rest of them did not show evidence of malignancy on biopsy tissue. Majority of non-malignant pathology specimen were reported as focal mild inflammation or chronic prostatitis. One patient's biopsy was reported as granulomatous prostatitis suggestive of Tuberculosis. 63% of patients had Gleason's score >7 and peri-neural invasion was seen in more than 81% of patients.

Pain during biopsy was minimal in majority of patients. On visual analogue scale (VAS), it was 2 or less in 84% patients.

Only five patients developed low grade fever after biopsy which subsided with antipyretics. None of them required hospital admission. A 71 year old man with multiple comorbidities, developed uro-sepsis and shock after prostate biopsy and required hospitalisation and ICU care.

Twenty patients noticed mild hematuria post biopsy which settled within two days. Only two patients had several episodes of gross hematuria lasting more than 2 days which ultimately resolved spontaneously. None of them required catheterization or bladder wash. None of the patients developed urinary retention following prostate biopsy. Six patients had hematochezia after biopsy which settled on its own.

Table 2: Complications following TRUS guided prostate biopsy (n= 34)

Minor Complications	
Minor complications low grade fever	5 (6.7%)
Hematuria <2 days	20 (26.4%)
Hematochezia	6 (8%)
Major complications	
Sepsis	1 (1.3%)
Hematuria >2 days	2 (2.7%)
Urinary retention	0

Amongst all prostate biopsy patients, 20 (27%) had a positive urine culture. E. coli (55%) was the most common organism followed by pseudomonas (20%).

Majority of the patients' cultures were found resistant to one or more of the eight most common antimicrobial agents used. Twelve (60%) were resistant to Cefpodoxime followed by resistance to Co-trimoxazole and Nitrofurantoin in 20%.

A subgroup analysis was carried out to look at factors which could predict occurrence of infection. Amongst the factors studied, only the presence of a positive urine culture pre-biopsy showed a statistically significant association with rate of infection. Though diabetics had a higher incidence of infection, it was not statistically significant. Similarly, presence or absence of an indwelling catheter did not contribute to post-biopsy infection.

Table 3: Risk factors for occurrence of infection following TRUS guided prostate biopsy

Factors	Present/ Absent	Rate of infection	*p* **value**
Urine culture	Positive	4/20 (20.0%)	0.040
	No growth or contaminants	2/55 (3.6%)	
Diabetes Mellitus	Present	2/18 (11.1%)	0.626
	Absent	4/57 (7.0%)	
Indwelling catheter	Present	0/10 (0%)	1.00
	Absent	6/65 (9.2%)	

Discussion

Trans rectal ultrasound guided prostate biopsy has remained the gold standard to diagnose prostate cancer. Biopsy related complications are not uncommon. Majority of the complications are mild and self-limiting but sometimes it could be severe and life threatening. Infection and bleeding from urethra and rectum are the most common complications following prostate biopsy.

To reduce the incidence of infection following biopsy, many prophylactic regimens including oral as well as intravenous antibiotics have been recommended by various studies (1,2). The class of antibiotic, dose and duration varies widely among centres. Most studies showed no significant benefit if duration is more than 24 hours (3,4,5). In our study, one dose of intravenous Injection Amikacin 15mg/kg was given just before biopsy in those whose urine culture showed no growth or contaminants. Otherwise patients received 3 days of culture specific antibiotics before biopsy, which was continued for a total of seven days.

We have not used any kind of rectal cleansing or enema before prostate biopsy. Cochrane review has also concluded that risk of bacteraemia was reduced with enema plus antibiotics when compared with antibiotics alone but risk of fever or infection was similar in both groups (6) Febrile UTI following prostate biopsy is common. Reported incidence rate of infection in different studies is around 3% (7,8). In our study, only one patient had febrile UTI which progressed to sepsis and required hospitalisation despite of being on antibiotics prior to procedure.

Incidence of fever reported in literature is about 3% to 3.5% (9,10). Our study had reported fever in 6% of patients, higher than reported in previous studies.

Hospitalisation rate in our study was 1.3%, similar to other studies in which it was 0.6% to 1.7% (11). But other studies have reported incidence of hospitalisation of 3.1% to 3.06% (7) Another study reported increase in hospitalisation rate from 1% to 4.1% from 1996 to 2005 (12).

Hematuria is very common following TRUS biopsy of prostate. Its incidence varies in literature from 10-84% (12,13). In a cohort study, incidence of hematuria was reported as

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65.8%, but bothersome hematuria was only 6.2% (13). Our study reported hematuria in 26.4% patients. But bothersome hematuria, lasting for more than 2 days was noted in only 2.7% patients. None of these patients required any intervention and it subsided spontaneously. A large prospective study on prostate cancer screening had reported prolonged hematuria (>3 days) in 22.6% and it correlated with prostate volume (9).

Incidence of hematochezia ranged from 1.3% and 45%. Studies have shown increased incidence of bleeding with increased number of biopsy cores and with use of anti-coagulative drugs (14). Our study did show an incidence of rectal bleeding of around 8%, all of which were self limiting.

TRUS guided prostate biopsy causes significant amount of pain. Therefore some form of analgesia is mandatory now. One study noted that TRUS biopsy prostate was associated with significant pain and discomfort as well as anxiety resulting in reluctance to subsequent biopsy, if required (13). There are other factors affecting pain during biopsy like rectal compliance, volume of prostate and number of prostate biopsy cores. Various types of anaesthesia/analgesia were described for prostate biopsy. Among them, peri-prostatic nerve block (PPNB) is safe and effective procedure. We performed prostate biopsy with patients in left lateral decubitus position and injected 10 ml of 1% Lignocaine as PPNB. It was very effective in reducing pain during biopsy and majority of our patients (84%) did not have clinically significant pain (based on VAS ≤2).

Risk of urinary retention following TRUS-Biopsy prostate is very small (0.2% to 1.7%). Number of cores taken during biopsy has no correlation with incidence of retention of urine. One study had assessed factors directly linked to retention of urine, including volume of prostate, transition zone volume to total prostate volume ratio and a higher score of IPSS (9,15,16). In our study, no patient had retention following prostate biopsy.

Overall, the risk of mortality is very low following prostate biopsy. Some studies have reported it less than 1% (12,17) Epidemiology and End Results. There was no death in our study.

Loeb S et al. have identified various risk factors for infectious complications after prostate biopsy. These include co-morbidities like Diabetes, COPD, Heart valve, benign prostate enlargement, recent urogenital infection, recent antibiotics, hospitalization, presence of a catheter, positive pre biopsy urine culture etc. (18)

The subgroup analysis of our study showed a statistically significant association between positive urine culture and rate of infection. This observation suggests that it would have been ideal to complete the course of antibiotic and document a sterile urine culture before proceeding for biopsy.

Another important correlation was made between diabetes and incidence of infection. Diabetes is a well established risk factor for increase incidence of infection following prostate biopsy (8,19,20)

Indwelling urethral catheter prior to biopsy was associated with low incidence of infection as compared to those who were voiding normally, although not statistically significant in our study population. Patients who were on urethral catheter, had a decompressed system and hence less likely to develop infection compared to patients with high residue.

Conclusion

Trans rectal ultrasound guided prostate needle biopsy is safe for diagnosing prostate cancer. The most common complication was hematuria in 26.4% of cases, followed by fever. Incidence of sepsis requiring hospitalisation was very low in our study. Increased incidence of infection in patients with positive urine culture suggests that treatment of infection and documentation of negative urine culture before biopsy may be wiser. Positive pre-biopsy urine culture and diabetes mellitus are risk factors which should be looked into before planning prostate biopsy.

References

1. Kapoor DA, Klimberg IW, Malek GH, Wegenke JD, Cox CE, Patterson AL, et al. Single-dose oral ciprofloxacin versus placebo for prophylaxis during transrectal prostate biopsy. Urology. 1998 Oct;52(4):552–8.
2. Gil-Vernet Sedo JM, Alvarez-Vijande García R. Effect of intrarectal povidone-iodine in the incidence of infectious complications after transrectal prostatic biopsy. Arch Esp Urol. 2012 May;65(4):463–6.
3. Sabbagh R, McCormack M, Péloquin F, Faucher R, Perreault J-P, Perrotte P, et al. A prospective randomized trial of 1-day versus 3-day antibiotic prophylaxis for transrectal ultrasound guided prostate biopsy. Can J Urol. 2004 Apr;11(2):2216–9.
4. Cam K, Kayikci A, Akman Y, Erol A. Prospective assessment of the efficacy of single dose versus traditional 3-day antimicrobial prophylaxis in 12-core transrectal prostate biopsy. Int J Urol Off J Jpn Urol Assoc. 2008 Oct;15(11):997–1001.
5. Shigemura K, Tanaka K, Yasuda M, Ishihara S, Muratani T, Deguchi T, et al. Efficacy of 1-day prophylaxis medication with fluoroquinolone for prostate biopsy. World J Urol. 2005 Nov;23(5):356–60.
6. Zani EL, Clark OAC, Rodrigues Netto N Jr. Antibiotic prophylaxis for transrectal prostate biopsy. Cochrane Database Syst Rev. 2011;(5):CD006576.
7. Wagenlehner FME, van Oostrum E, Tenke P, Tandogdu Z, Çek M, Grabe M, et al. Infective complications after prostate biopsy: outcome of the Global Prevalence Study of Infections in Urology (GPIU) 2010 and 2011, a prospective multinational multicentre prostate biopsy study. Eur Urol. 2013 Mar;63(3):521–7.
8. Simsir A, Kismali E, Mammadov R, Gunaydin G, Cal C. Is it possible to predict sepsis, the most serious complication in prostate biopsy? Urol Int. 2010;84(4):395–9.
9. Raaijmakers R, Kirkels WJ, Roobol MJ, Wildhagen MF, Schrder FH. Complication rates and risk factors of 5802 transrectal ultrasound-guided sextant biopsies of the prostate within a population-based screening program. Urology. 2002 Nov;60(5):826–30.
10. Djavan B, Ravery V, Zlotta A, Dobronski P, Dobrovits M, Fakhari M, et al. Prospective evaluation of prostate cancer detected on biopsies 1, 2, 3 and 4: when should we stop? J Urol. 2001 Nov;166(5):1679–83.
11. Zaytoun OM, Anil T, Moussa AS, Jianbo L, Fareed K, Jones JS. Morbidity of prostate biopsy after simplified versus complex preparation protocols: assessment of risk factors. Urology. 2011 Apr;77(4):910–4.
12. Nam RK, Saskin R, Lee Y, Liu Y, Law C, Klotz LH, et al. Increasing hospital admission rates for urological complications after transrectal ultrasound guided prostate biopsy. J Urol. 2013 Jan;189(1 Suppl):S12–17; discussion S17–18.
13. Rosario DJ, Lane JA, Metcalfe C, Donovan JL, Doble A, Goodwin L, et al. Short term outcomes of prostate biopsy in men tested for cancer by prostate specific antigen: prospective evaluation within ProtecT study. BMJ. 2012;344:d7894.
14. Ghani KR, Dundas D, Patel U. Bleeding after transrectal ultrasonography-guided prostate biopsy: a study of 7-day morbidity after a six-, eight- and 12-core biopsy protocol. BJU Int. 2004 Nov;94(7):1014–20.
15. Pinkhasov GI, Lin Y-K, Palmerola R, Smith P, Mahon F, Kaag MG, et al. Complications following prostate needle biopsy requiring hospital admission or emergency department visits - experience from 1000 consecutive cases. BJU Int. 2012 Aug;110(3):369–74.

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16. Berger AP, Gozzi C, Steiner H, Frauscher F, Varkarakis J, Rogatsch H, et al. Complication rate of transrectal ultrasound guided prostate biopsy: a comparson among 3 protocols with 6, 10 and 15 cores. J Urol. 2004 Apr;171(4):1478–81.
17. Loeb S, Carter HB, Berndt SI, Ricker W, Schaeffer EM. Complications after prostate biopsy: data from SEER-Medicare. J Urol. 2011 Nov;186(5):1830–4.
18. Loeb S, Vellekoop A, Ahmed HU, Catto J, Emberton M, Nam R, et al. Systematic review of complications of prostate biopsy. Eur Urol. 2013 Dec;64(6):876–92.
19. Carignan A, Roussy J-F, Lapointe V, Valiquette L, Sabbagh R, Pépin J. Increasing risk of infectious complications after transrectal ultrasound-guided prostate biopsies: time to reassess antimicrobial prophylaxis? Eur Urol. 2012 Sep;62(3):453–9.
20. Loeb S, van den Heuvel S, Zhu X, Bangma CH, Schröder FH, Roobol MJ. Infectious complications and hospital admissions after prostate biopsy in a European randomized trial. Eur Urol. 2012 Jun;61(6):1110–4.