OPEN ACCESS Freely available online

Medical & Surgical Urology

Research Article

Hematuria after Transrectal Prostate Biopsy: A Warning of Future Infection

Alan Quach, Colin I. O'Donnell, Mohammed Al-Musawi, Simon Kim, Tracey MacDermott, Al Barqawi*

Department of Surgery, Division of Urology, Denver School of Medicine, University of Colorado, Colorado, United States

ABSTRACT

Purpose: To identify the incidence and predictive factors of infectious complications in a prophylactic-controlled cohort of men undergoing transrectal ultrasound-guided prostate needle biopsy (TRUS-Bx) at a single institution.

Materials and Methods: A retrospective review was performed on 539 patients who underwent TRUS-Bx between 2010-2015. All patients received prophylactic Sulfamethoxazole/Trimethoprim and Levofloxacin prior to the biopsy. Charlson Comorbidity Index (CCI) was calculated for each patient. The characteristics of patients with and without infectious complications were compared using Fisher exact tests and student's t-test.

Results: 539 biopsies were performed. Mean age was 64 years, PSA was 17, prostate volume was 41 mL, and CCI score was 3. A total of 7 (1.3%) infectious complications were reported 48-72 hours after biopsy, with 2 (0.4%) developing sepsis. Analysis indicated no significant differences in mean age (p=0.544), PSA (p=0.881), prostate volume (p=0.532), or CCI score (p=0.499) among patients who developed infection. Individual components of the CCI revealed no statistically significant differences. Additional complications following biopsy included: hematuria (8.3%), rectal bleeding (1.3%), urinary urgency (0.9%), and new onset erectile dysfunction (0.6%). Hematuria was associated with the development of infectious complications (OR=8.75, CI 1.895–40.400, p=0.0055).

Conclusions: Our cohort of patients undergoing TRUS-Bx had a lower infectious rate compared to that reported by the AUA (1.1% vs 5-7%). Although this study has limited power, CCI was poorly predictive of infectious complications following TRUS-Bx. Persistent hematuria following biopsy was associated with infectious complications. The clinical importance of hematuria following TRUS-Bx, if any, needs to be further clarified.

Keywords: TRUS; Complications; Charlson comorbidity index; Risk factors

INTRODUCTION

Transrectal ultrasound-guided prostate biopsy is a commonly practiced elective procedure for detecting prostate cancer with a relatively low chance of sepsis (0.6-5.7%) [1,2]. Other post biopsy complications include hematuria (50%), rectal bleeding (30%), hematospermia (50%), urinary retention (0.2-2.6%), and erectile dysfunction (<1%). However, a rise in the infection rate associated with TRUS-Bx has been reported in recent years [1-3]. In general, the risk factors for post procedural infection are categorized as related to antibiotic resistance, patient characteristics, and procedure related factors [4].

Bacteria inoculation of the urinary tract is thought to be the result of penetrating trauma from the rectum to the prostate caused by the needle during core biopsy. The use of antibiotic prophylaxis, despite being the main strategy to prevent infection [5-7], may have declining efficacy as recent studies point to antibiotic resistance as the main cause of the increasing infection rates, with Escherichia coli (E.coli) being the most frequent causative bacteria followed by Klebsiella pneumonia and Klebsiella oxytoca [1,4,8,9]. E. coli, compared to other common bacterial flora, was found to be most resistant to fluoroquinolones, sulfonamides, and penicillins. Klebsiella pneumonia was found to be resistant to fluoroquinolones, sulfonamides, nitrofuran, and aminoglycosides [10]. Recent literature proposes different empiric antibiotic prophylaxis protocols, including variable combinations of fluoroquinolones, penicillins, aminoglycosides, cephalosporins, nitrofurantoin and

***Correspondence to:** Al B. Barqawi, Department of Surgery, Division of Urology, Denver School of Medicine, University of Colorado, Colorado, United States, Tel: 303-724-2722; E-mail: Al.Barqawi@cuanschutz.edu

Received date: June 06, 2020; **Accepted date:** July 20, 2020; **Published date:** July 27, 2020

Citation: Quach A, O'Donnell CI, Al-Musawi M, Kim S, MacDermott T, Barqawi AB (2020) Voiding Troubles, Fecal Incontinence and Anal Intercourse. Med Sur Urol 9:233. doi: 10.24105/2168-9857.9.233

carbapenem [11]. The use of targeted antibiotic prophylaxis based on culture and sensitivity results is more specific and has shown improvement in infection rates [2,6].

Patient characteristics associated with higher risk for infection include diabetes, high Charlson Comorbidity score, recent hospitalization, presence of indwelling urinary catheter, and recent international travel [2,4,12]. Patients with diabetes are associated with elevated renal parenchymal glucose levels setting a favorable environment for microbial growth [13]. Significant comorbidities such as chronic kidney disease is associated with poor prognosis and increased susceptibility to infection. Prior hospitalizations increase the likelihood of exposure to resistant microbes and subsequent antibiotic prophylaxis failure. Indwelling catheters are known to serve as a nidus for urinary tract infections (UTI). Other factors that may increase the risk of infection includes immunosuppression and comorbidities requiring immunosuppressive therapy due to weakened immunity. Additionally, prior history of prostate biopsy infection predisposes patients to reinfection after subsequent biopsies [14].

In addition to antibiotics, modified procedural techniques to prevent infection such as povidone iodine preparation of the rectal mucosa [15] and use of one biopsy needle for each biopsy puncture [7] have been successful in reducing infection rates in small cohorts. Bowel preparation protocol prior to prostate biopsy had previously been shown to reduce infectious rates but it is still debated as more recent studies have found no statistically significant reduction in infectious complications [16].

In our study, we aim to measure the incidence of infectious complications in a prophylactic-controlled cohort of men undergoing TRUS-Bx in our institution, and identify factors associated with higher risk of post procedural infection. We also intend to evaluate whether these factors can be used to predict patient vulnerability to postoperative infection and may benefit from a targeted prophylactic strategy to minimize their risk of infection [6].

MATERIAL AND METHODS

A retrospective chart review was performed on 539 consecutive patients who underwent TRUS-Bx between 2010-2015. All biopsies included in this study were completed with fixed routine procedures performed by the same surgeon. All patients received a prophylactic antibiotic regimen 24 hours prior to biopsy with two doses of oral Sulfamethoxazole/Trimethoprim 500 mg and one dose of oral Levofloxacin 500 mg 15 minutes prior to biopsy. Aspirin and anticoagulation was withheld seven days prior to biopsy. Patients requiring continued prophylaxis were bridged to Enoxaparin. At least 15 minutes prior to TRUS guided biopsy, urinalysis was ordered and elevation in any infectious laboratory values required rescheduling after urine cultures showed no growth. All staff involved in the procedure wore sterile gloves. Single use lubricating gel containers were emptied onto the sterile field prior to the operation. Single use needle guides were used during the procedure. No rectal swab or prophylactic enemas were performed. All biopsies were completed with a BK ultrasound system. Patients are instructed to call our clinic or go to the emergency department immediately should they have any high fevers, shaking chills, or flu like symptoms. Furthermore, all patients were contacted by nursing staff within seven days post-procedure to review their recovery and specifically ask about the following symptoms: bleeding, pain, dysuria, difficulty urinating, fever or chills. Within 14 days of biopsy date, patients were again contacted with pathology results and questioned again about post-procedure complications. An infectious outcome was defined as a patient who verbalized these symptoms during follow up phone call or presented to any emergency department or our clinic with suspected infection or urine culture confirmed infection related to the genitourinary tract or where no other etiology of infection was evident within seven days of TRUS biopsy.

Patient data, including demographic, procedural and patient-related factors were collected on a standardized form using hospital records. Charlson Comorbidity Index (CCI) data was calculated for each patient. We indicated elevated comorbidity in patients with a CCI >1. Twelve needle core biopsies were taken guided by real time ultrasound imaging. The biopsy cores were taken in the standard fashion including six from the right and six from the left prostatic hemispheres.

Comparisons of patient characteristics and comorbidities between those with and without infection were obtained by Fisher exact tests and student's t-tests. Multivariable logistic regression requires between five and ten events per adjustment covariate, with some experts suggesting 15 events just to obtain an intercept. With only seven infections in the cohort, there were too few events to perform a logistic regression.

Data from this study has previously been presented as a poster "Predictive Factors of Infectious Complications Following Transrectal Ultrasound-Guided Prostate Needle Biopsy" at the South Central Section Conference of the American Urology Association in 2018. The title of the study has been modified since.

RESULTS

539 biopsies were performed. Mean age was 64 years, PSA was 17, prostate volume was 41 mL, and CCI score was 3. A total of 7 (1.3%) infectious complications were reported with 2 patients (0.4%) developing sepsis. Analysis indicated no significant differences in mean age (p=0.544), PSA (p=0.881), prostate volume (p=0.532), or CCI score (p=0.499) among patients who developed infection (Table 1). Additionally, individual components of the CCI revealed no statistically significant differences (Table 2). Additional complications following biopsy included: hematuria (8.3%), rectal bleeding (1.3%), urinary urgency (0.9%), and new onset erectile dysfunction (0.6%) (Table 3). Hematuria was associated with the development of infectious complications (OR=8.75, CI 1.895 – 40.400, p=0.0055). The Charlson Comorbidity Index Score >1 was not associated with infectious complications (OR=1.1409, CI 0.1356-9.5981, p=0.9034). Our report includes 32 patients who had two biopsies and five patients who underwent three biopsies. Of this subgroup with a prior history of TRUS-Bx, one patient had an infectious complication during his first biopsy

without recurrence in his second biopsy. A total of 265 (49%) patients were found to have positive biopsies (defined as one or more cores with the presence of malignant cells). Five out of seven patients (71%) that developed infectious complications were also diagnosed with prostate cancer. This finding did not show any statistically significant association between positive biopsy results and post-operative infectious complications (OR = 2.62, CI 0.503-13.600, p=0.25).

Table 1: Baseline Characteristics.

Characteristic	Overall Patients (N=539)	Patients who did not develop infection (N=532)	Patients who developed infection (N=7)	P-Value
Age, years, mean ± SD	64.5 ± 7.4	64.4 ± 7.4	66.1 ± 5.9	0.54
Prostate volume, cc, mean ± SD	41.0 ± 22.7	41.0 ± 22.8	35.6 ± 10.8	0.53
PSA, ng/mL, mean ± SD	17.4 ± 153.2	17.6 ± 154.2	8.8 ± 6.3	0.88
Charlson Comorbidity Index, mean ± SD	3.0 ± 1.8	3.0 ± 1.8	3.3 ± 2.3	0.67
Biopsy cores, mean ± SD	11.7 ± 1.9	11.7 ± 1.9	12 ± 0.0	0.64

Table 2: Components of Charlson Comorbidity Index as Predictors of Infection.

Charlson Comorbidity Index Factor	Factor present, patients with infection	Factor present, patients without infection	Odds Ratio	95% CI	P-Value
Myocardial Infarction	0	14	0	0-21.436	1.00
Congestive Heart Failure	0	6	0	0-56.847	1.00
Peripheral Vascular Disease	0	13	0	0-23.273	1.00
Cerebrovascular Disease	1	12	7.22	0.145-66.746	0.16
Dementia	0	0	-	-	-
Chronic Obstructive Pulmonary Disease	0	14	0	0-21.436	1.00
Connective Tissue Disease	0	1	0	0-1444.0	1.00
Peptic Ulcer Disease	0	1	0	0-1444.0	1.00
Mild Liver Disease	0	2	0	0-279.648	1.00
Diabetes Mellitus	2	75	2.44	0.228-15.186	0.26
Hemiplegia	0	0	-	-	-
Chronic Kidney Disease	0	44	0	0-6.093	1.00
Diabetes Mellitus w/ organ damage	0	18	0	0-16.254	1.00
Tumor	2	138	1.14	0.108-7.071	1.00
Lymphoma	0	1	0	0-1444.0	1.00
Leukemia	0	0	-	-	-

Moderate-Severe Liver Disease	1	15	5.74	0.117-51.870	0.19
Metastatic Tumor	0	1	0	0-1444.00	1.00
AIDS	0	2	0	0-279.648	1.00

Table 3: Procedural Complications as Predictors of Infection.

	Cohort (n=539)	Factor present, patients with infection (n=7)	Factor present, patients without infection (n=532)	Odds Ratio	95% CI	P-Value
Rectal Bleeding	7 (1.3%)	0	7	0	0-47231	1.00
Hematuria	45 (8.3%)	3	42	8.75	1.230-53.138	0.02
Urethral Meatal Stricture	0 (0.0%)	0	0	-	-	-
Urinary Urgency	5 (0.9%)	0	5	0	0-71.292	1.00
New Onset Erectile Dysfunction	3 (0.6%)	0	3	0	0-173.304	1.00
Charlson-Comorbidity Index Score >1	453 (84.04)	6	447	1.1409	0.1357-53.09	1.00

DISCUSSION

The rates of total prostate biopsies and PSA testing have declined by 33% from 2005 to 2014 (17) and by 36.8% from 2010 to 2013(18), respectively. This is likely due to the 2008 release of key updates in prostate specific antigen (PSA) screening guidelines in the US Preventive Services Task Force (USPSTF) recommendations as well as the 2013 American Urological Association (AUA) guidelines. These updates recognized the lower-than-expected utility in PSA for prostate cancer screening in the general population and increased morbidity due to false positive and subsequent tests. Contrary to expectations due to recent decline in numbers of biopsies, those that underwent the procedure had an increase in complication rates, primarily driven by infectious complications [17]. These findings indicate a need to recognize modifiable factors in infectious complications in cases in which prostate biopsies are indicated.

Visible hematuria and infection are known complications of TRUS-guided prostate biopsy with incidence reported between 2-84% and 5-7% respectively [14,18,19]. The wide incidence range for hematuria is likely a result of varying study definitions of hematuria and timing cutoffs. It is generally considered a minor complication that is expected to be self-limiting. The prevalence of infectious complications found in 1.1% of this current cohort was lower than the AUA reported range of 5-7%. Certainly, differences in techniques and prophylactic antibiotic regimen could contribute to the rate differences between the present study and that reported by the AUA. Though it would be difficult to tease out individual procedural factors that attributes to this discrepancy, all biopsies included in this study were completed with fixed routine procedures performed by the same surgeon. Adherence to standard principles of infection control and proper sterilization of equipment was a priority. Notable protocols in this study include strict sterilization of operators and equipment, urinalysis prior to the procedure, single use lubrication and needles. Targeted prophylactic therapy based on rectal swab culture has been studied and shown to reduce infectious and septic complications [20]. This cohort was provided with a fixed prophylactic dose and frequency of Sulfamethoxazole/Trimethoprim and Levofloxacin. In our literature review of rectal cleansing with enemas prior to procedures, we found conflicting results related to reduced infectious outcomes. A double blinded, randomized study on 280 men undergoing TRUS-Bx found a statistically significant reduction in infection in their bowel preparation group versus the control [21]. On the other hand, AbuGhosh et al. studied a larger cohort of 865 men who had prophylactic rectal cleansing with povidone iodine prior to biopsy. They found a relative risk reduction of 42% compared to patients that did not receive a prophylactic rectal cleaning, though this reduction was not shown to have any statistical significance [22]. Pre-biopsy enemas and rectal swab cultures were not utilized in our practice. Furthermore, several studies have noted a recent exposure to antibiotics is associated with increased risk of severe infection [23,24]. Data from this cohort did not include history of antibiotic exposure and was thus excluded from the study design.

Additionally, our data is noted to have lower incidence of complications associated with hematuria (8.3%), rectal bleeding (1.3%) and new onset erectile dysfunction (0.6%). For a better comparison of complication rates with that found on the AUA White Paper, future studies should include the same parameters at multiple randomized institutions. Our study did not find any statistically significant predisposition to infectious complications in patients who have had a prior post TRUS-biopsy UTI as there were no patients in the cohort with this specific timeline. This coincides with similar findings from Djavan et al. which showed no statistical significance in infectious outcomes (p=0.07) when comparing patients ' first and repeat TRUS-Bx [23]. Furthermore, a sizeable proportion of our cohort with infectious outcomes were found to have positive prostate biopsies (71%). However, without sufficient power, it is difficult to make conclusions based on this finding in our study. This relationship has been analyzed by Sfanos et al. resulting in a high degree of bacterial DNA (87%) found in the prostates of men with prostate cancer [24]. It has been hinted by other studies that there may be an association between chronic inflammatory processes from infection and the development of prostate cancer [25]. Interestingly, E. Coli has also been identified in a small proportion of patients with BPH [26]. Despite the mounting evidence of a relationship between prostate disease and infection, the pathophysiology behind prostatic disease and infection has yet to be explained.

Our findings in this 5-year retrospective study of 539 patients suggest an association between post-operative hematuria and urinary tract infections (p<.01). While hematuria is a symptom of urinary tract infection with a likelihood ratio of 1.72 and high specificity [27], it has not been extensively studied whether or not one complication predisposes to another in the setting of post TRUS-Bx. In our study, three patients presented to the emergency department or outpatient clinic with complaints of both lower urinary tract symptoms and hematuria. It is unclear whether one preceded the other. All three patients improved with antibiotic and/or supportive treatment without any further complications. Although the literature lacks clarity behind the pathophysiology of infection in post-TRUS biopsy, it is likely due to direct exposure of bacteria from the rectum to previously isolated systems (i.e. blood vessel, prostate, urinary tract) [3]. In a similar process, hematuria is thought to be a result of direct trauma from a core needle penetrating into the prostate and subsequent sloughing of blood into the urethra.

In a nationwide Swedish study of over 50,000 men, high patient Charlson Comorbidity Scores as well as diabetes were found to be risk factors for infectious outcomes after TRUS-Bx. Data was extracted from a national registry for patients with diagnosed prostate cancer. As such, that study did not comment on overall infectious outcomes from TRUS-Bx as patients with negative biopsies were excluded. Prophylactic antibiotic regimen and sterilization protocol was not standardized [12]. According to another Swedish study, current national guidelines suggest 10-12 TRUS-guided core biopsies without any further operative standardization [28]. In our smaller cohort study from a single provider and standardized procedures, it is likely that various factors (i.e. technique, sterilization, bowel prep, variation in antimicrobial prophylaxis) play a role in the contrasting findings.

Although our data is limited by a small number of patients with infectious complications, our analysis indicates patient comorbidity and prior diagnosis of diabetes are not statistically significant predictors of infectious outcomes. Moreover, this cohort is limited by a much smaller sample size in comparison to the Swedish study which limits the statistical power for detecting significant findings. Thus, while unnecessary TRUS biopsy should be avoided, when necessary, proper evaluation should not be omitted for concern of infectious complications in patients with increased comorbidities or those with diabetes.

CONCLUSION

Our cohort of patients undergoing TRUS guided prostate biopsy had a notably reduced rate of post-operative infections, when compared to that of the AUA (1.1% vs 5-7%). Although the reason behind this is unclear and needs to be further studied, we believe our lower prevalence is related to a strictly sterile protocol. Furthermore, the Charlson Comorbidity Index was poorly predictive of infectious complications following TRUS-Bx. Patients who reported persistence of hematuria within 48 to 72 hours following biopsy had higher odds of developing infectious complications. The exact clinical importance of hematuria following TRUS biopsy, if any, needs to be clarified further.

FUNDING

There is no financial support or formal funding (i.e. grants, sponsors) for this study.

CONFLICTS OF INTEREST

The authors declare that there is no conflict of interest regarding the publication of this paper.

SUMMARY

Diabetes, high Charlson Comorbidity score, recent hospitalization, presence of indwelling urinary catheter, and recent international travel has been noted to increase infectious complications in patients undergoing TRUS-Bx. This study fixes pre-biopsy and biopsy protocol and reports a lower than expected (when comparing to reported averages) rate of infectious outcomes. Furthermore, we observed that the presence of hematuria after TRUS-Bx was associated with infection. However, we did not find a significant association between elevated Charlson Comorbidity scores (or its individual components) with infectious complications. These findings may suggest the need for an increased degree of surveillance in patients that report hematuria in the first few days after biopsy. Furthermore, proper evaluation for prostate cancer via TRUS-Bx should not be omitted for concern of infectious complications in patients with increased comorbidities.

REFERENCES

1. Lee SJ. Infection after transrectal ultrasound-guided prostate biopsy. Korean journal of urology 2015; 56:346-350.

2. Anderson E, Leahy O, Cheng AC. Risk factors for infection following prostate biopsy - a case control study. BMC infectious diseases 2015; 15:580.
3. Neulander EZ, Yusim I, Kaneti J. Re: increasing hospital admission rates for urological complications after transrectal ultrasound guided prostate biopsy. J Urol 2010; 183:963-969.
4. Carignan A, Roussy JF, Lapointe V. Increasing risk of infectious complications after transrectal ultrasound-guided prostate biopsies: time to reassess antimicrobial prophylaxis? European urology 2012; 62:453-459.
5. Auffenberg GB, Qi J, Gao Y. Evaluation of a needle disinfectant technique to reduce infection-related hospitalisation after transrectal prostate biopsy. BJU international 2018; 121:232-238.
6. Cussans A, Somani BK, Basarab A. The role of targeted prophylactic antimicrobial therapy before transrectal ultrasonography-guided prostate biopsy in reducing infection rates: a systematic review. BJU international 2016; 117:725-731.
7. Qiu XF, Yang GS, Chen BT. One-puncture one-needle TRUS-guided prostate biopsy for prevention of postoperative infections. Zhonghua nan ke xue = National journal of andrology 2017; 23:630-634.
8. Zaytoun OM, Vargo EH, Rajan R. Emergence of fluoroquinolone-resistant Escherichia coli as cause of postprostate biopsy infection: implications for prophylaxis and treatment. Urology 2011; 77:1035-1041.
9. Loeb S, van den Heuvel S, Zhu X. Infectious complications and hospital admissions after prostate biopsy in a European randomized trial. European urology 2012; 61:1110-1114.
10. AlKhateeb SS, AlShammari NA, AlZughaibi MA. The prevalence of urinary tract infection, or urosepsis following transrectal ultrasound-guided prostate biopsy in a subset of the Saudi population and patterns of susceptibility to flouroquinolones. Saudi medical journal 2016; 37:860-863.
11. Webb NR, Woo HH. Antibiotic prophylaxis for prostate biopsy. BJU international 2002; 89:824-828.
12. Lundström K-J, Drevin L, Carlsson S. Nationwide Population Based Study of Infections after Transrectal Ultrasound Guided Prostate Biopsy. Journal of Urology 2014; 192:1116-1122.
13. Schneeberger C, Kazemier BM, Geerlings SE. Asymptomatic bacteriuria and urinary tract infections in special patient groups: women with diabetes mellitus and pregnant women. Current opinion in infectious diseases 2014; 27:108-114.
14. Liss MA, Ehdaie B, Loeb S. An Update of the American Urological Association White Paper on the Prevention and Treatment of the More Common Complications Related to Prostate Biopsy. The Journal of urology 2017; 198:329-334.
15. Allen JL, Lehman K, Dewan K. Procedural povidone iodine rectal preparation reduces bacteriuria and bacteremia following prostate needle biopsy. The Canadian journal of urology 2017; 24:8883-8889.
16. Ruddick F, Sanders P, Bicknell SG. Sepsis rates after ultrasound-guided prostate biopsy using a bowel preparation protocol in a community hospital. Journal of ultrasound in medicine: official journal of the American Institute of Ultrasound in Medicine 2011; 30:213-216.
17. Gershman B, Van Houten HK, Herrin J. Impact of Prostate-specific Antigen (PSA) Screening Trials and Revised PSA Screening Guidelines on Rates of Prostate Biopsy and Postbiopsy Complications. European urology 2017; 71:55-65.
18. Jemal A, Ma J, Siegel R. Prostate Cancer Incidence Rates 2 Years After the US Preventive Services Task Force Recommendations Against Screening. JAMA oncology 2016; 2:1657-1660.
19. Loeb S, Vellekoop A, Ahmed HU. Systematic review of complications of prostate biopsy. European urology 2013; 64:876-892.
20. Duplessis CA, Bavaro M, Simons MP. Rectal cultures before transrectal ultrasound-guided prostate biopsy reduce post-prostatic biopsy infection rates. Urology 2012; 79:556-561.
21. Ghafoori M, Shakiba M, Seifmanesh H. Decrease in infection rate following use of povidone-iodine during transrectal ultrasound guided biopsy of the prostate: a double blind randomized clinical trial. Iran J Radiol 2012; 9:67-70.
22. AbuGhosh Z, Margolick J, Goldenberg SL. A Prospective Randomized Trial of Povidone-Iodine Prophylactic Cleansing of the Rectum Before Transrectal Ultrasound Guided Prostate Biopsy. Journal of Urology 2013; 189:1326-1331.
23. Djavan B, Waldert M, Zlotta A. Safety and morbidity of first and repeat transrectal ultrasound guided prostate needle biopsies: results of a prospective European prostate cancer detection study. The Journal of urology 2001; 166:856-860.
24. Sfanos KS, Sauvageot J, Fedor HL. A molecular analysis of prokaryotic and viral DNA sequences in prostate tissue from patients with prostate cancer indicates the presence of multiple and diverse microorganisms. The Prostate 2008; 68:306-320.
25. Sfanos KS, Isaacs WB, De Marzo AM. Infections and inflammation in prostate cancer. Am J Clin Exp Urol 2013; 1:3-11.
26. Bergh J, Marklund I, Thellenberg-Karlsson C, Gronberg H. Detection of Escherichia coli 16S RNA and cytotoxic necrotizing factor 1 gene in benign prostate hyperplasia. European urology 2007; 51:457-462.
27. Giesen LGM, Cousins G, Dimitrov BD. Predicting acute uncomplicated urinary tract infection in women: a systematic review of the diagnostic accuracy of symptoms and signs. BMC Fam Pract 2010; 11:78.
28. Carlsson S, Bratt O, Stattin P, Egevad L. Current routines for transrectal ultrasound-guided prostate biopsy: A web-based survey by the Swedish Urology Network. Scandinavian Journal of Urology and Nephrology 2012; 46:405-410.