นิพนธ์ต้นฉบับ

ปัจจัยที่ทำนายภาวะแทรกซ้อนจากการตัดชิ้นเนื้อต่อมลูกหมากผ่านทางทวารหนัก

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บทคัดย่อ

วัตถุประสงค์ : เพื่อประเมินว่าปัจจัยใดบ้างที่จะเป็นตัวบ่งชี้ถึงภาวะแทรกซ้อนที่รุนแรงหลังจากการใช้เข็มตัดชิ้นเนื้อต่อมลูกหมากผ่านทางทวารหนักโดยใช้อัลตราซาวน์นำทาง

ผู้ป่วยและวิธีการศึกษา : เป็นการศึกษาแบบไปข้างหน้าในกลุ่มผู้ป่วย 688 คนที่สงสัยว่าเป็นมะเร็งต่อมลูกหมากและได้รับการใช้เข็มตัดชิ้นเนื้อต่อมลูกหมากผ่านทางทวารหนักโดยใช้อัลตราซาวน์นำทาง ในโรงพยาบาลศิริราช ระหว่างเดือนกรกฎาคม พ.ศ.2553 - ตุลาคม พ.ศ.2554 แล้วนำข้อมูลที่ได้ไปคำนวณทางสถิติ

ผลการศึกษา : พบผู้ป่วยมีภาวะแทรกซ้อนที่รุนแรง 27 คน (ร้อยละ 3.9) ซึ่งประกอบด้วย มีการติดเชื้อ 12 คน (ร้อยละ 1.7 โดย 3 คน มีภาวะต่อมลูกหมากอักเสบ, 3 คนมีภาวะท่อนำอสุจิและอัณฑะอักเสบ 7 คน มีการติดเชื้อทางเดินปัสสาวะที่มีไข้, 1 คนมีภาวะติดเชื้อในกระแสโลหิต) ภาวะเลือดออกที่รุนแรง 8 คน (ร้อยละ 1.1; โดย 6 คน มีภาวะปัสสาวะเป็นเลือดออกรุนแรง 2 คน มีภาวะอุจจาระเป็นเลือด และหมดสติ (vagovagal reflex) 7 คน (ร้อยละ 1.0) ปัจจัยที่พบว่าทำให้เกิดภาวะแทรกซ้อนที่รุนแรงที่มีความสำคัญอย่างมีนัยสำคัญทางสถิติ คือ การระงับความรู้สึกระหว่างตัดชิ้นเนื้อโดยฉีดยาชาที่เส้นประสาทข้างต่อมลูกหมากและจำนวนชิ้นเนื้อที่ตัดมากกว่า 20 ชิ้น

สรุป : ไม่มีการเสียชีวิตเกิดขึ้นจากการใช้เข็มตัดชิ้นเนื้อต่อมลูกหมากผ่านทางทวารหนักในการศึกษานี้ และพบว่า การระงับความรู้สึกระหว่างตัดชิ้นเนื้อโดยฉีดยาชาที่เส้นประสาทข้างต่อมลูกหมากและจำนวนชิ้นเนื้อที่ตัดมากกว่า 20 ชิ้น เป็นปัจจัยที่ทำให้เกิดภาวะแทรกซ้อนที่รุนแรง

คำสำคัญ : ปัจจัยเสี่ยง ตัดชิ้นเนื้อต่อมลูกหมากผ่านทางทวารหนัก ฉีดยาชาที่เส้นประสาทข้างต่อมลูกหมาก

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Original Article

Factors predicting complications after transrectal ultrasound guided prostate biopsy

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Abstract

Objective: To evaluate risk factors of major complications after transrectal ultrasound guided prostate biopsy.

Materials and Methods: 688 patients who were suspected to have prostate cancer and underwent transrectal ultrasound-guided prostate biopsy (TRUS and Biopsy) at Siriraj hospital between July 2010 to October 2011 were enrolled in the study. The parameters of demographic data, antibiotic prophylaxis, patients preparation, biopsy technique and complications after procedure were recorded.

Results: Major complication occurred in 27 patients (3.9%). These complications were as follows: infection in 12 patients (1.7%; three were acute prostatitis, three was epididymo-orchitis, seven were febrile urinary tract infection and one was urosepsis), bleeding in 8 patients (1.1%; six were massive hematuria, two were massive hematochezia) and vasovagal syncope in 7 patients (1.0%). Statistically significant risk factor were periprostatic nerve block and core number of needle biopsies more than 20 core.

Conclusion: There was no mortality after TRUS and biopsy in this study. Periprostatic nerve block and core number of needle biopsies; more than 20 core were the risk factor of the major complications.

Keywords: risk factor, transrectal ultrasound-guided prostate biopsy, periprostatic nerve block

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Introduction

Prostate cancer is the fifth most common malignancy in the world and is also the second most common cancer in men[1]. PSA testing, widely used to diagnose for early stage prostate cancer, causes an increasing rate of prostate needle biopsies[2].

Definitive diagnosis of prostate cancer can be established through histological evaluation of prostate tissue. In the past, Ferguson obtained prostatic tissue which was aspirated with an 18-gauge needle via the transperineal approach[3]. Later, Astraldi first performed the transrectal approach, which has replaced the old approach[4]. At present, transrectal ultrasonography guided 10 to 12 cores biopsy is the gold standard and is used routinely for prostate cancer diagnosis[5]. Although, transrectal ultrasonography guided biopsy (TRUS-guided biopsy) is generally safe and well tolerated on an out-patient basis, it is still an invasive procedure associated with some potential risk and morbidity[6]. Approximately 2% of patients who undergo this procedure will developd a febrile urinary tract infection and bacteremia requiring hospitalization for intravenous antibiotics[7].

In the past, many studies analyzed risk factors for major complications after TRUS-guided biopsy. For instance, Raaijmarkers et al. reported an increasing number of core biopsies correlated with hemorrhage and infection. Bladder catheterization, however, was also a risk factor for infection[8]. On the other hand, Buerger et al. demonstrated that a higher number of core biopsies did not increase the incidence of major complications[9]. Furthermore, Lee et al. also reported that bladder catheterization was not a factor for major complications after TRUS-guided biopsy[10].

Currently, there is no conclusion concerning the risk factors of TRUS-guided biopsy complications. Therefore, this study aims to evaluate the risk factors predicting complications from TRUS-guided biopsy at Siriraj Hospital.

Material and Methods

Six hundred and eighty-eight patients who underwent a TRUS-guided biopsy were enrolled between July 2010 and October 2011 at Siriraj Hospital. Indications for prostate biopsy in this study were high serum PSA level (more than 4 ng/ml), and/or abnormal digital rectal examination. TRUS-guided biopsies performed on patients simultaneously with other urologic procedures, including transurethral resection of prostate and cystoscopy, were excluded from study.

All patients were informed about the TRUS-guided biopsy and all potential complications before they were scheduled for the procedure. All consented to the procedure. Pre-procedure preparations, including antibiotic regimen and mechanical bowel preparation, were provided individually for each patient. The preparation undertaken depended upon the urologist who performed the procedure. Antiplatelets such as aspirin, were discontinued under agreement with the cardiologist for at least one week prior to the procedure.

TRUS-guided biopsies were performed in both the out-patient and in-patient departments. In the out-patient settings, all of the biopsies were performed under local anesthesia with vital signs monitoring for one hour. For in-patient settings, all patients were given general anesthesia and admitted for observation, if patients had multiple underlying diseases, or had requested that the procedure be performed under general anesthesia, they were admitted to the hospital for biopsy and observation.

The instruments used for TRUS-guided biopsy are a spring loaded biopsy gun, 18-gauge Tru-cut needle and Pro-Focus 2202, and a 12 MHz biplane

ultrasound. Prostate gland volume was measured and automatically calculated before the biopsy. A TRUS-guided biopsy was performed on all of the patients in the left lateral decubitus position with flexion of the hip and both knees. The volume of the prostate gland was measured and the number of core biopsies varied according to each urologists decision.

Pre-procedure data, including blood pressure, heart rate, and all demographic data, were collected. Post-procedure data, including blood pressure, heart rate, and pain scale scores during the procedure were collected using the visual analog pain scale. All patients received instructions about completing a self-accessed complications chart in order to assess themselves. They would returned for the pathologic report approximately 2 weeks after the procedure. Complications were recorded by the patients using the self- accessed complications chart and through interviews with the patients at appointments or by phone. If the patients had any abnormal symptoms, such as fever or bleeding, they were advised to return to the hospital within 48-72 hours after the symptoms presented themselves.

The results were analyzed with PASW statistics 18 edition. The data were analyzed by independent t-test or Mann-Whitney U test for continuous data and the Chi-square test or Fisher's exact test for categorical data. Logistic regression analysis was used to determine a significant complication factor which was defined as a p-value less than 0.05.

Results

Demographic data are shown in Table 1. There were 688 patients enrolled in this study. Two hundred two (29.4%) patients were diagnosed with prostate cancer.

Complications were divided into major and minor groups. Major complications were defined as complications after TRUS-guided biopsy that required prolonged hospitalization (in-patient group) or when the patient required hospitalization (out-patient group) and/or close observation. Complications which followed transrectal ultrasound guided prostate biopsy are shown in Table 2.

The major complications were divided into infectious complications (prostatitis, epididymo orchi-

Table 1 Demographic data (N=688) of the patients

	Number (%)
Age (years) - Mean±SD	67.2±7.8
BMI(kg/m^2) - Mean±SD	24.1±3.1
PSA level(ng/ml) - Median (Min-Max)	9.44 (0.03-3,482.0)
Prostate volume(cm3) - Median (Min-Max)	38.3 (8.41-157)
Underlying disease	613 (89.1%)
Hypertension	119 (17.3%)
Diabetes mellitus	380 (55.2%)
Benign prostate hyperplasia	367 (53.3%)
History previous TRUS-guided biopsy	172 (25.1%)
History previous prostate surgery	30 (4.7%)
Lower urinary tract symptom	461 (68.3%)

tis, UTI with fever, urosepsis), hemorrhage complications (gross hematuria and hematochezia that required hospitalization or prolong admission), and vasovagal syncope.

Of the 27 (3.92%) patients who had major complications, 14 underwent TRUS-guided biopsy on an out-patient basis and required hospitalization, with a length of hospital stay of 2-17 days. There were 9 patients who had TRUS-guided biopsy under general anesthesia who experienced major complications with a prolonged hospital stay of greater than the usual 1-9 days. There was no mortality in this study.

Major complications and possible risk factors are shown in Table 3. This table shows the types of anesthesia used during the procedures. The numbers of core biopsies were statistically significant for major complications. Logistic regression analyses were used to test and significantly determine the complication factors, as shown in Table 4. Periprostatic nerve block and the core number of needle biopsies (more than 20 cores) were statistically significant in major complications after TRUS-guided biopsy.

Infectious complications were the ones most frequently found among major complications; the most severe infectious complication in this study was

Table 2 Major and minor complications following TRUS-guided biopsy

Complication	Number (n=688)
Major complication	27 (3.9%)
Infection	
UTI with fever	7(25.9%)
Prostatitis	3(11.1%)
Epididymo orchitis	3(11.1%)
Urosepsis	1(3.7%)
Hemorrhage	
Massive gross hematuria	6(22.2%)
Massive hematochezia	2(7.4%)
Vasovagal syncope	7(25.9%)
Minor complication	626 (92.6%)
Infection	
Dysuria	74 (11.8%)
Fever less than 48 hr	19 (3%)
Hemorrhage	
Gross hematuria	525 (83.6%)
Hematochezia	284 (46%)
Hematospermia	36 (5.7%)
Others	
Anorectal discomfort	286 (45.5%)
Acute urinary retention	30 (4.7%)

Table 3 Shows possible risk factors for complications in TRUS-guided biopsy

Risk factors	Total	Complication	p-value
Present urethral catheter before TRUS-guided biopsy			1.000
No	655	26 (4%)	
Yes	25	1 (4%)	
Fleet enema before TRUS-guided biopsy			0.298
No	120	7 (5%)	
Yes	561	2 (3.6%)	
Type of Anesthesia			<0.001
No pain control	407	8 (2%)	
Periprostatic nerve bladder	69	11 (15.9%)	
General Anesthesia	205	8 (3.9%)	
Prostate volume (cm^3)			0.240
≤ 45	344	9 (2.6%)	
> 45	223	10 (4.5%)	
Number of core biopsies			0.002
≤ 12	429	9 (2.1%)	
13-20	237	15 (6.3%)	
> 20	22	3 (13.6%)	
Antibiotic prophylaxis			0.547
oral route	82	4 (4.9%)	
intravenous plus oral route	586	22 (3.8%)	
Povidone-Iodine cleaned rectum before TRUS-guided biopsy			0.381
No	191	10 (52%)	
Yes	490	17 (3.5%)	

Table 4 Logistic regression analysis of the number of core biopsies and type of anesthesia

Risk factors	Odds ratio	95% CI of odds ratio
Number of core biopsies		
≤ 12	1	
13-20	1.11	0.34-3.64
> 20	6.06	1.22-29.98
Type of anesthesia		
No pain control	1	
Periprostatic nerve block	6.86	2.09-22.55
General Anesthesia	1.79	0.64-5.06

urosepsis, which is by definition a systemic inflammatory response syndrome (SIRS)* with signs of bacterial infection. There was one urosepsis in this study.

Minor complications were found in 626 (92.6%) patients; gross hematuria was the most common and accounted for 76.3%. These hematuria were self-limited with a duration of 1-12 days. Fifty-one patients (7.4%) in this study were complication-free.

* SIRS is defined by the presence of 2 or more criteria from a collection of clinical signs and laboratory investigations as follows:

- Temperature >38.3°C or <36.0°
- Tachycardia >90 beats/ minute
- Tachypnoea >20 breaths/minute or $PaCO_2$ less than 32 mm Hg
- White blood cell count >12,000 cell/cm^3 or 4,000 cell/cm^3), or >10% immature (band) forms.[11]

Discussion

TRUS-guided biopsy is a simple and accurate method to receive prostatic tissue for histologic evaluation. Previous studies[7,9,12-14] have shown a variation in the number of complications using this technique as reviewed in Table 5. Major complications in this study were 3.92%, which is comparable to other studies ranging from 3.5% to -6.6%[9,12-14]. Our minor complications were 92.6% where as other studies range from 53.1% to 73.3%[9,12,14]. It should be noted that there was no well defined criteria for minor complications. Our study found a small group of patients had hematospermia (5.7%), which was low compared to other studies 7.2% to-50.4%[12-14]. This could be because our patients had less frequent sexual intercourse and some patients did not ejaculate at all for 2 weeks following the procedure. If our study had a longer follow-up period, more hematospermia may have been found[6,9,12,15].

Therefore, the factors predicting complications are

1. Present urethral catheter before TRUS-guided biopsy

Previous studies report the presence of bladder catheterization as a risk factor for infectious complications after TRUS-guided biopsy[8]. It is possible that the presence of a catheter indwelling, a foreign body in the urinary tract, leads to the proliferation of pathogenic microorganism[8]. In contrast, this study shows no association between bladder catheterization and major complications. However, the results in this study may not be conclusive because of the small number of patients with urethral catheter indwelling before their procedures.

2. Fleet enema before TRUS-guided biopsy

Rectal preparation is not routinely used prior to TRUS-guided biopsy. In the United Kingdom, 18% of patients had an enema before the TRUS-guided biopsy[17]. Asymptomatic bacteraemia after prostate biopsy was commonly found and could be minimized by pre-biopsy enema independent of antibiotic administration[18]. This study found that fleet enemas were not associated with major complications. However Bisacodyl for rectal preparation, before TRUS-guided biopsy can decrease the complication rate[14]. Nevertheless this study shows no significant decrease in complications due to various bowel preparations, e.g., nothing per oral, senokot, soft soap enema, emulsion liquid paraffin compound (ELPco), milk of magnesia and mucillin which may decrease bacterimia .

3. Periprostatic nerve block

TRUS-guided biopsy in an outpatient setting can cause discomfort and some degree of pain. Several studies show that local anesthesia can reduce pain effectively while patients undergo an TRUS-

Table 5 Review of complications and risk factors after TRUS-guided biopsy

Authors	Year	Sample size(n)	Study design	Biopsy core (n)	Hospitalization (%)	UTI (%)	HU (%)	HS (%)	HC (%)	Risk Factor for major complication
DJavan et al.[16]	2001	1,051	prospective	8	NA	10.9	15.9	9.8	2.1	-
Raaijmarkers et al.[12]	2002	5,676	prospective	6-7	0.5	6.9	22.6	50.4	1.3	-
Raaijmarkers et al.[8]	2004	174	prospective	3-17	2.3	9.2	56.3	21.8	32.3	Bladder catheterization and increase number of core biopsy
Chiang et al.[13]	2007	1,875	retrospective	6-15	6.6	NA	1.9	NA	0.2	Prostate size > 45 ml
Lee et al.[10]	2009	1,529	retrospective	6	3.2	1.4	4.1	1.1	0.9	Pre-biopsy UTI and rectal preparation
Present study	2013	688	prospective	3-36	3.0	1.0	77.0	5.2	41.3	Periprostatic nerve block and core biopsy > 20 cores

UTI = Urinary tract infection; HU = hematuria; HS = hematospermia; HC = hematochezia; NA = not available

guided biopsy[19-21]. Two anesthetic strategies were used (periprostatic nerve block: PNB, General anesthesia: GA) in this study in order to reduce the pain associated with TRUS-guided biopsy.

PNB in our study was performed using 1-2% of Lidocaine without adrenaline, injected into the prostate via the rectum by a long spinal needle 18 gauge (at the bilateral region of the prostatic vascular pedicle) just lateral to the junction between the prostate and seminal vesicle, 4 ml on each side, and the apex of the prostate 2-4 ml. In our study, PNB tends to decrease pain when compared with the non PNB group. Visual analog pain scale scores in the PNB and non PNB group were 3.01 and 3.60 respectively. However, PNB was associated with major complications (UTI with fever and vasovagal syncope), which might be explained by injuries to other structures unseen by the doctor during the procedure due to poor picture quality. PNB can cause injury to other structures and lead to UTI with fever. Infiltration of a soluble substance by an extra needle (spinal needle) punctures through the rectum that had high bacterial colonization and high vascular space directly correlates to infection complications[21]. Moreover vasovagal syncope may become an adverse effect of xylocaine, e.g., hypotension, bradycardia and dizziness22.

4. Prostate volume > 45 cm^3

In our study, there were no major complications when the prostate volume was > 45 cm^3, which is contrary to Chiang et al[13]. This may be explained by our good preparation of patients before their biopsy.

Prostate volume that increased in size was associated with an increased severity of lower urinary tract symptoms. Therefore, acute urinary retention after TRUS-guided biopsy may be caused by prostatic tissue injury, resulting in prostatic swelling.

5. Number of core biopsies

Although an increased number of core biopsies may improve the cancer diagnostic yield, there are concerns about increased pain and morbidity[23]. Core needle biopsies of more than 20 cores are also related to major complications. Multiple core needle biopsies increase the probability of infectious complications because of the increased chance of introducing rectal bacteria to the prostate and circulation[8,24]. However, Berger, Naughton et al. found that extended core biopsies (8-12, 10 and 15 cores) were not associated with major complications. The result of this study is the converse of ours, the converse of ours. We performed more core biopsies in our study; this could be the cause of the discrepancy in the two results[9,15].

6. Antibiotic prophylaxis (intravenous plus oral route versus oral route)

Infection is the most common major complication of prostate biopsy. Antibiotic prophylaxis administration significantly reduces urinary tract infection after TRUS-guided biopsy[7,9,12]. The drug of choice for preoperative antibiotic prophylaxis remains controversial. Various regimens regarding the antibiotic prophylaxis were used and the routes have been studied[17,24,25]. In this study, we compared pre-operative antibiotics via parenteral and oral route versus oral route alone. The result is not significant but analysis was precluded due to the multiple regimens of antibiotic prophylaxis used by individual surgeons. This study was not designed to compare the 2 groups."

7. Povidone-Iodine cleaned rectum prior to TRUS-guided biopsy

Povidone-iodine is in widespread use in medical practice because it has broad-spectrum antimicrobial activity, including those against viruses, fungus and parasites[26]. Rectal preparation with povi-

done-iodine suppository prior to prostate biopsy can control rectal bacterial colony-forming units and species effectively[26]. However, cleaning the rectum with povidone-iodine prior to TRUS-guided biopsy has no statistical significance because other factors may have an effect, such as the use of hibitane (an antibacterial cleanser) to clean the rectum, rectal preparation, and use of pre-operative antibiotics to decrease bacteremia.

The limitation of this study is the use of the self-assessed complication chart, which some patients forgot to return on their follow-up. Therefore, a recall bias occurred. Moreover, there were too many protocols among surgeons who performed antibiotic prophylaxis prior to TRUS-guided biopsy.

Conclusion

TRUS-guided biopsy is the gold standard for tissue diagnosis of prostate cancer. The procedure is considered safe, however, major complications can arise. Periprostatic nerve block and more than 20 core needle biopsies were risk factors for major complications. This knowledge may help to reduce major complications in the future, and aid in counseling patients who plan to undergo TRUS-guided biopsy.

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