ORIGINAL ARTICLE

Major Complications and Associated Risk Factors of Transrectal Ultrasound Guided Prostate Needle Biopsy: A Retrospective Study of 1875 Cases in Taiwan

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Background/Purpose: Complications from transrectal ultrasound (TRUS) guided prostate needle biopsy are occasionally encountered in the daily practice of urologists. We tried to determine the associated risk factors of patients who suffered from major complications that required hospitalization after TRUS guided prostate needle biopsies.

Methods: We did a retrospective review of 1875 TRUS guided prostate biopsies performed between January 2002 and December 2005. We defined major complications as patients with complications that needed hospitalization. We analyzed the association between biopsy complications and suspected factors, including age, prostate volume, patient's underlying disease, selection of prophylactic antibiotics, biopsy core numbers (6, 12, and 15 cores), and antiplatelet/anticoagulant usage.

Results: There were 124 patients (6.6%) with major complication. These major complications were categorized as acute prostatitis (3.8%), acute urinary retention (2.1%), hematuria (1.9%), rectal bleeding (0.2%), epididymitis (0.2%), sepsis (0.05%), and vasovagal syncope (0.05%). Patients with larger prostate size were noted to have higher risk of developing transient acute prostatitis and acute urinary retention after prostate biopsy. In contrast, age, prophylactic antibiotics (levofloxacin and pipemidic acid), underlying diseases (diabetic mellitus, hypertension, hyperlipidemia, cerebrovascular accident, coronary artery disease), increased biopsy core numbers, and antiplatelet/anticoagulant usage were not associated with major complications after prostate biopsy.

Conclusion: TRUS guided prostate needle biopsy is a safe diagnostic tool in most elderly males with or without systemic underlying disease. [*J Formos Med Assoc* 2007;106(11):929–934]

Key Words: complications, morbidity, risk factors, transrectal ultrasound prostate needle biopsy, TRUS

Transrectal ultrasound (TRUS) guided prostate needle biopsy is the standard diagnostic procedure for detecting prostate cancer. Since the late 1980s, prostate specific antigen (PSA) has been used for the screening of prostate cancer. TRUS guided prostate needle biopsy became one of the most common procedures in the daily practice of urologists.[1] Although TRUS guided prostate needle biopsy is generally considered to be a safe and easy procedure, complications are occasionally encountered. In previous literature, Berger et al reported 5957 prostate biopsies performed from

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Received: March 22, 2007
Revised: June 26, 2007
Accepted: August 7, 2007

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1993 to 2002 in Austria, retrospectively. Minor complications included hematospermia (36.3%), hematuria (14.5%) and rectal bleeding that persisted for up to 2 days (2.3%).[2] Major complications included fever (0.8%), rectal bleeding requiring surgical intervention or persisting for more than 2 days (0.6%) and urinary retention (0.2%). Djavan et al reviewed previous reports of complications after TRUS prostate needle biopsy. Immediate and delayed complications were reported, including urinary tract infection (1.2–11.3%), fever (1.4–4.5%), sepsis (0.1–0.3%), hematuria (12.5–58.4%), hematospermia (5.1–45.3%), rectal bleeding (2.1–37.1%), urinary retention (0.2–2.6%), and voiding difficulty (6.7–13.7%).[3] Complication rates were variable probably due to different definitions of complication by authors. The incidence and mortality rate of prostate cancer have gradually increased with industrialization in Taiwan.[4] The usage of TRUS prostate biopsies may progressively increase with the importance of prostate cancer screening. Thus, we did a retrospective study of 1875 TRUS guided prostate needle biopsies from a single institution in Taiwan and tried to determine the associated risk factors of patients who suffered from major complications that needed hospitalization after TRUS guided prostate needle biopsies.

Methods

We did a retrospective study by reviewing the medical records of 1875 TRUS guided prostate biopsies performed in a single institution between January 2002 and December 2005. The predominant indication for biopsy was an increased PSA level and/or abnormal digital rectal examination. Rectal preparation with bisacodyl was performed 6 hours before biopsy. Patients with antiplatelet/anticoagulation agents were instructed to discontinue aspirin 7 days before biopsy and to discontinue warfarin 3 days before biopsy. Between January 2002 and December 2004, patients received pipemidic acid 500 mg twice daily for 3 days from the day of biopsy. Between January 2005 and December 2005, patients received levofloxacin 500 mg single dose on the morning before biopsy.

Patients' variables, including age, prostate volume, prophylactic antibiotics, underlying diseases, biopsy core numbers, pathologic results, and antiplatelet (aspirin)/anticoagulant (warfarin) usage were assessed. We defined major complications as patients with complications that needed hospitalization. These major complications were categorized as fever, hematuria, acute urinary retention, rectal bleeding, epididymitis, sepsis, and vasovagal syncope. Results were analyzed with commercial statistical software and p values were calculated with χ^2 test, t test, ANOVA, and logistic regression. Statistically significant difference was defined as $p < 0.05$.

TRUS examinations were performed with a real-time ultrasound scanner (B&K 1846 model) using a 7-MHz transducer. Prostate volume was calculated from the TRUS image using the formula volume (mL) = 0.52 × length × width × height (cm). Patients were placed in the left decubitus position. Biopsies were done with 18G tru-cut biopsy needles during longitudinal scanning. The procedure was performed by eight chief residents alternatively with attendings' supervision.

Results

A total of 1875 TRUS guided prostate biopsies were performed between January 2002 and December 2005; 1199 patients (63.9%) received prostate biopsy during admission and 676 patients (36.1%) received prostate biopsy at the outpatient clinic. There were 536 (28.58%) patients who were diagnosed with prostate cancer.

Complications

Of the 1875 TRUS guided prostate needle biopsies, 124 patients (6.6%) were noted to have major complications that needed further hospitalization. These major complications were 3.8% acute prostatitis (55 of 1875), 2.1% acute urinary retention (39), 1.9% hematuria (36), 0.2%

rectal bleeding (4), 0.2% epididymitis (4), 0.05% sepsis (1), and 0.05% vasovagal syncope (1).

Age

Of the 1875 TRUS guided prostate needle biopsies, patients' age was between 45 and 94 years. The mean age of patients was 67.3 ± 10.2 years. In the group of patients with major complications (C Group), their mean age was 68.0 ± 11.4 years. In the group of patients without major complications (NC Group), their mean age was 67.2 ± 10.1 years. There was no significant difference in patient age identified between patients with (C Group) and without major complications (NC Group) ($p = 0.407$).

Volume

The range of prostate volume was from 11.3 to 176 mL. Mean prostate volume was 44.7 ± 22.3 mL. The mean prostate volume in the C Group was 52.6 ± 26.0 mL, while it was 44.1 ± 21.9 mL in the NC Group. There was a significant difference in prostate volume between patients with (C Group) and without major complications (NC Group) ($p = 0.001$). By reviewing likelihood ratio statistics and areas under the curve from logistic regression models to complication occurrence, prostate volume was analyzed using indicator variables for each 5 mL, and the cut-off point with the largest area under the curve was 45 mL. Patients with a prostate volume greater than 45 mL (8.1%) were more likely to suffer from biopsy complications than patients with prostate volume less than 45 mL (6.0%) ($p < 0.05$).

Major complications were further divided into fever (acute prostatitis), acute urinary retention, hematuria, rectal bleeding, epididymitis, sepsis, and vasovagal syncope. There was significant difference in prostate volume measured between patients with and without acute prostatitis ($p = 0.001$) and acute urinary retention ($p = 0.019$) (Figure). In contrast, there was no significant difference in prostate volume measured between patients with/without hematuria, epididymitis, rectal bleeding, and others ($p > 0.05$).

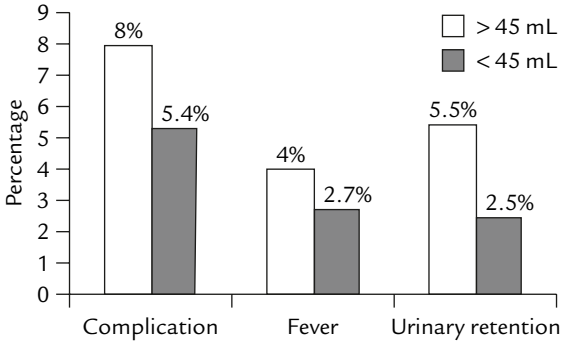

Figure. Comparison of complication rate between prostate volume greater and less than 45 mL.

Core numbers of needle biopsies

Of the 1875 TRUS guided prostate needle biopsies, 931 patients received the standard sextant biopsy (6 core), 841 patients received sextant and lateral biopsy (12 core), and 84 patients received sextant combined lateral biopsy, and additional nodule biopsy (15 core). There were 59 patients with major complications in the 6-core group (59/931, 6.34%), 58 patients with major complications in the 12-core group (58/841, 6.9%), and five patients with major complications in the 15-core group (6/84, 6.95%). There was no significant difference in complication rates among the 6-, 12- and 15-core groups ($p > 0.05$).

Prophylactic antibiotics

Between January 2002 and December 2004, 1373 patients received pipemidic acid 500 mg twice daily for 3 days from the day of prostate biopsy. Between January 2005 and December 2005, 502 patients received levofloxacin 500 mg single dose on the morning before biopsy. There were 96 patients with major complications in the pipemidic acid group (96/1373, 7%) and 28 patients with major complications in the levofloxacin group (28/502, 5.6%). There was no significant difference in total complication rate between the pipemidic acid and levofloxacin groups ($p > 0.05$). The infection complication rates were 3.27% and 1.99% in the pipemidic acid and levofloxacin groups, respectively. There was no significant difference in infection rate with the different antibiotics ($p > 0.05$).

Antiplatelet medication and anticoagulant

Of the 1875 TRUS guided prostate needle biopsies, 180 patients received antiplatelet medication and anticoagulants: 173 received aspirin and seven have received warfarin. Aspirin was discontinued 7 days before biopsy. Warfarin was discontinued 3 days before biopsy. Complication rate after prostate biopsy was 8.9% in all patients who received antiplatelet medication and anticoagulant, 10% in the aspirin group, and 0% in the warfarin group. There was no significant difference in complication rate after prostate biopsy between patients with/without aspirin or warfarin usage with adequate period of discontinuation ($p > 0.05$).

Underlying diseases

Of the 1875 TRUS guided prostate needle biopsies, there were 130 patients with diabetes mellitus (DM), 315 patients with hypertension, 133 patients with hyperlipidemia, 44 patients with previous cerebrovascular disease (CVA), 213 patients with coronary artery disease (CAD), and 61 patients with hepatic disease. Complication rate after prostate biopsy was 6.2% in the DM group, 7.4% in the hypertension group, 9% in the hyperlipidemia group, 7.6% in the CVA group, 8% in the CAD group, and 11.5% in the hepatic disease group. There was no significant difference in complication rate after prostate biopsy between patients with and without these underlying diseases ($p > 0.05$) (Table).

Discussion

In this retrospective study of 1875 cases, with regard to age, prostate volume, prophylactic antibiotics, underlying diseases, biopsy core numbers, and antiplatelet (aspirin)/anticoagulant (warfarin) usage, we noted that prostate volume was the only risk factor that was associated with major complications after TRUS guided prostate needle biopsy. There was significant difference in prostate volume measured between patients with (C Group, 52.6 ± 26.0 mL) and without major complications (NC Group, 44.1 ± 21.9 mL). A prostate volume of 45 mL was identified as the cut-off value that indicated which patients would be more prone to having post-biopsy complications. Raaijmakers et al evaluated 5802 patients who received TRUS prostate needle biopsies in the Netherlands.[5] They reported minor complications, including hematuria for more than 3 days (22.6%) and hematospermia (50.4%), as well as major complications, including fever (3.5%) and urinary retention (0.4%). Their risk factor analysis yielded prostate volume, transition zone volume/total prostate volume ratio, and a higher International Prostate Symptom Score, as predictors of urinary retention. Our results are compatible with those of their study. After dividing major complications into fever (acute prostatitis), hematuria, acute urinary retention, rectal bleeding, epididymitis and others, there was a significant difference in prostate volume measured between patients with and without

Table. Potential risk factors and complication rates

Risk factor	Complication rate (%)		*p*
	+	−	
Diabetes mellitus	6.2	6.6	0.50
Hypertension	7.6	6.5	0.45
Cerebrovascular accident	7.7	6.5	0.16
Coronary artery disease	8.0	6.4	0.38
Hepatic disease	11.1	6.5	0.18
Aspirin	10.0	6.3	0.11
Warfarin	6.6	0	1.00
Biopsy cores	6	12	15
Complication rate (%)	6.34	6.90	6.95

acute prostatitis ($p = 0.001$) and acute urinary retention ($p = 0.019$). In contrast, there was no significant difference in prostate volume measured between patients with and without hematuria, epididymitis, rectal bleeding and others ($p > 0.05$). This information was of little value in clinical decisions, because it is not acceptable to hold prostate biopsy due to large prostate size. Sech et al have reported interexaminer differences in prostate volume measurement with TRUS. However, total prostate volume reliability was higher for prostate volume > 40 mL.[6] Thus, we could inform patients with larger prostate size in advance that there might be a higher risk of developing transient acute prostatitis and acute urinary retention after prostate biopsy.

In our study, the complication rate did not increase with biopsy core numbers. There was no significant difference between protocols with 6, 12 and 15 cores. Berger et al also compared complication rate of protocols with 6, 10 and 15 biopsy cores and found no difference.[2]

There has been debate about antibiotic prophylaxis of TRUS prostate needle biopsy.[7–12] Different regimens with different routes, dosage, duration and different costs are available. Enlund and Varenhorst stated that antibiotic prophylaxis might not be necessary.[13] They did 415 prostate biopsies without prophylactic antibiotics. Complication rate of fever was 2.9%, which did not far exceed the complication rate of fever in other studies. Taylor and Bingham recommended oral ciprofloxacin or norfloxacin with/without metronidazole.[7] Griffith et al proposed that a single dose of 500 mg levofloxacin represented excellent infection prophylaxis of TRUS guided prostate biopsy with low infection rate because levofloxacin, one of the new generation of quinolones, is highly effective against Gram-negative organisms, which are the most common pathogens responsible for infection after biopsy.[14] We have adopted the simple and convenient regimen suggested by Griffith et al since 2005 due to the low infection rate in their study. In our study, the total complication rate (7% *vs.* 5.6%) and infection rate with acute prostatitis (3.2% *vs.* 1.99%) showed no significant difference between 3-day usage of pipemidic acid and a single dose of levofloxacin.

The efficacy of decreasing infection rate with rectal enema has been a topic of debate in the literature. Lindert et al conducted a prospective randomized study, which proposed that enema before biopsy may decrease bacteremia and bacteriuria after prostate biopsy.[15] All of the patients in our study received rectal preparation with bisacodyl based on the opinion of Lindert et al. Thus, there was no control group without enema in our study.

In consideration of antiplatelet and anticoagulant usage in the elderly, we studied the association between aspirin/warfarin usage and post-biopsy complication rate. We noted that if patients were instructed to discontinue aspirin for 7 days and coumadin for 3 days before biopsy, then the complication rate would not increase in this group.

There is no previous literature discussing comorbidity and complication rate. In our study, we found that patients with hypertension, DM, CVA, CAD, and hepatic disease did not have higher risks of complications after TRUS guided prostate needle biopsy.

In conclusion, TRUS guided prostate needle biopsy is a safe diagnostic tool in most elderly males with and without systemic underlying disease. The only risk factor associated with prostate biopsy was large prostate size. Patients with prostate volume > 45 mL should be informed of the increased complication rate of having post-biopsy acute prostatitis and urinary retention. Age, prophylactic antibiotics (levofloxacin and pipemidic acid), underlying diseases (DM, hypertension, hyperlipidemia, CVA, CAD), increased biopsy core numbers, and antiplatelet/anticoagulant usage were not associated with major complications after prostate biopsy.

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