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Original Article

Transrectal ultrasound-guided prostate biopsy in Taiwan: A nationwide database study

Tzu-Chun Wei [a,b], Tzu-Ping Lin [a,b,*], Yen-Hwa Chang [a,b], Tzeng-Ji Chen [c], Alex T.L. Lin [a,b], Kuang-Kuo Chen [a,b]

[a] *Department of Urology, Taipei Veterans General Hospital, Taipei, Taiwan, ROC*
[b] *Department of Urology, School of Medicine, and Shu-Tien Urological Institute, National Yang-Ming University, Taipei, Taiwan, ROC*
[c] *Department of Family Medicine, Taipei Veterans General Hospital, Taipei, Taiwan, ROC*

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Abstract

Background: For patients with an elevated prostate specific antigen (PSA) level or a suspected lesion detected by digital rectal examination, transrectal ultrasound-guided (TRUS) prostate biopsy is the standard procedure for prostate cancer diagnoses. In Taiwan, TRUS prostate biopsy has not been well-studied on a nationwide scale. This article aimed to study TRUS prostate biopsy in Taiwan and its related complications, according to the claims generated through the National Health Insurance (NHI) program.

Methods: We applied for access to claims from the NHI Research Database of Taiwan of all patients who visited the urology clinic during the period of 2006 to 2010. In the 5-year urology profile, we obtained all records, which included admission and ambulatory clinical records. The definition of TRUS biopsy included codes for ultrasound-guided procedure and for prostate puncture; other codes involving complications such as postbiopsy voiding difficulty, significant bleeding, or infection requiring treatment were also included. Risk factors included age, diagnosis of prostate cancer, hospitalization or nonhospitalization, and the Charlson Comorbidity Index (CCI; with a value of 0, 1, 2 or ≥ 3). Descriptive and comparative analyses were also performed.

Results: In the 5-year urology profile, 12,968 TRUS biopsies performed of which 6885 were in-patient procedures and 6083 were ambulatory clinic procedures. After the procedures, 1266 (9.76%) biopsies were associated with voiding difficulty; 148 (1.14%) biopsies, with significant bleeding; and 855 (6.59%) biopsies, with infection that required treatment. The prostate cancer diagnosis rate was 36.02%. The overall biopsy-related mortality rate within 30 days was 0.25%, and the postbiopsy sepsis-related mortality rate was 0.13%. Age, diagnosis of cancer, hospitalization, and CCI value ≥ 1 were all significant factors in univariate analysis and multivariate analysis for postbiopsy voiding difficulty and severe infection. A diagnosis of cancer and a CCI value ≥ 2 were significant factors for significant bleeding after biopsy. Patients diagnosed as having prostate cancer had fewer bleeding complications after biopsy.

Conclusion: The most frequent complication was postbiopsy voiding difficulty, followed by infection that required treatment and significant bleeding. The sepsis-related mortality rate was 0.13%. Significant risk factors for postbiopsy complications included age, diagnosis of prostate cancer, hospitalization, and the CCI value.

Keywords: complication; National Health Insurance; research database; Taiwan; transrectal ultrasound-guided prostate biopsy

Conflicts of interest: The authors declare that there are no conflicts of interest related to the subject matter or materials discussed in this article.

* Corresponding author. Dr. Tzu-Ping Lin, Department of Urology, Taipei Veterans General Hospital, 201, Section 2, Shih-Pai Road, Taipei 112, Taiwan, ROC.
E-mail address: tplin@vghtpe.gov.tw (T.-P. Lin).

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1. Introduction

National Health Insurance (NHI) in Taiwan has been in effect since May 1995, and the coverage rate is 99% of the population.[1] Since 1999, the Bureau of the NHI has established two types of databases that are subgroups of the larger National Health Insurance Research Database (NHIRD). One database is the random sampled database comprising ambulatory visits or admission datasets; the other database is a special database generated by requests for selected criteria such as patients having specific diseases or undergoing specific procedures or medications. By analyzing the National Health Insurance Research Database (NHIRD), a nationwide view of specific clinically significant problems can be scrutinized.

For patients with elevated prostate specific antigen (PSA) levels or suspected lesion detected by digital rectal examination, transrectal ultrasound-guided (TRUS) prostate biopsy is the standard procedure for the diagnosis of prostate cancer. The incidence and prevalence rate of prostatic disease has increased because of the phenomenon of an aging population in Taiwan.[2] However, prostate cancer has a variable clinical course, and a significant proportion of prostate cancer cases may be indolent cancer. Thus, some patients with prostate cancer may die *with* it rather than die *of* it. There is also a study that demonstrates that extended biopsy improves the concordance of the Gleason scores between biopsy and prostatectomy, which indicates it has more complication risks.[3] Therefore, whether to check the PSA level in elderly men as a screening device for cancer has always been subject to debate, especially when considering complications associated with TRUS biopsy.[4–7] Our investigation aimed to study TRUS prostate biopsy and related complications in Taiwan, based on the claims of the NHI program.

2. Methods

From the NHIRD of Taiwan, we applied the data of all claims of patients who ever visited a urology clinic during the period of 2006–2010. In the resulting 5-year urology profile, we received all records from both admission (DO and DD files) and ambulatory clinics (OO and CD files). Codes for the ultrasound-guided procedure (19007B or 19002B) and the prostate puncture (29028C or 79401C) in combination were used to define TRUS biopsy.

Post-TRUS biopsy complications included voiding difficulty, significant bleeding, or infection requiring treatment. Postbiopsy voiding difficulty was indicated by an indwelling catheterization code after biopsy. Postbiopsy significant bleeding was defined as incidents necessary to be managed with endoscopic hemostatic procedures or transfusion. Infection that required treatment was defined by intravenous antibiotic administration for at least six dosages, and an admission period longer than 3 days, either during the admission of the biopsy or during the first admission within 7 days after biopsy.

The following risk factors were included: age, diagnosis of prostate cancer (heavy disease verification file, 185), hospitalization or nonhospitalization (i.e., biopsy performed either through admission or ambulatory clinics), and Charlson Comorbidity Index value[8] (CCI; values are 0, 1, 2, and ≥3).

Descriptive and comparative analyses were performed using SPSS version 17.0 software (SPSS Inc., Chicago, IL, USA). Relative risks were assessed by using Chi square or logistic regression tests in univariate analysis and multiple regression for multivariate analysis. This study was approved and certified by the Institutional Review Board (Taipei Veterans General Hospital, Taipei, Taiwan).

3. Results

In the 5-year urology profile, 12,968 TRUS biopsies were detected. The mean age of patients at the time of biopsy was 69.9 years (Fig. 1). Among the procedures, 6885 biopsies were performed during hospitalization and 6083 biopsies were performed at ambulatory clinics (Table 1); 4671 (36.02%) patients were diagnosed as having prostate cancer, which was confirmed by linkage to the heavy disease verification (HV) file. Thirty-two patients died within 30 days after biopsy (0.25% biopsy-related mortality); of these, 17 patients had an infection that required treatment (i.e., 0.13% biopsy-related sepsis-induced mortality).

Among the 12,968 TRUS prostate biopsies, 1266 (9.76%) patients had postbiopsy voiding difficulty (Table 2), which required the use of am indwelling Foley catheter. One hundred and forty-eight (1.14%) patients who underwent transfusion or endoscopic management also had significant bleeding (Table 3). Eight hundred and fifty-five (6.59%) patients who

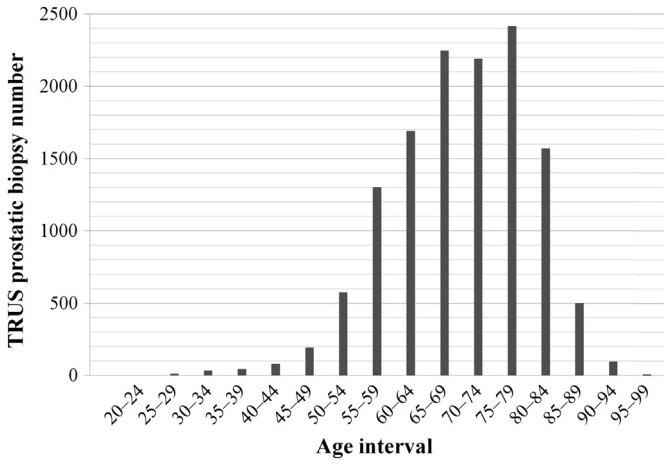

Fig. 1. Age distribution of the patients (representing 12,968 prostatic biopsies). The mean age is 69.9 years. TRUS = transrectal ultrasound-guided.

Table 1
Clinical data for all 12,968 prostatic biopsies, based on genitourinary service.

Admission (n = 6885)		Ambulatory visit (n = 6083)	
GU (n = 6457)	Not GU (n = 455)	GU (n = 6081)	Not GU (n = 2)
Malignancy diagnosis			36.0
Postbiopsy 30-d mortality			0.25
Biopsy-related sepsis-induced mortality			0.13

All data are presented as %.
GU = genitourinary department application.

Table 2
Risk factors for voiding difficulty after TRUS biopsies.

Risk factor	Voiding difficulty (9.76%)					
	Univariate RR	95% CI	*p*	Multivariate RR	95% CI	*p*
Age	1.04	1.03–1.05	<0.001	1.02	1.01–1.03	<0.001
Prostate ca.	1.53	1.37–1.73	<0.001	1.17	1.01–1.34	0.032
Admission	9.01	7.27–11.16	<0.001	5.60	4.78–6.55	<0.001
CCI ≥1	2.29	1.77–2.97	<0.001	1.38	1.05–1.81	0.020

Admission = admission for TRUS biopsy; CCI = Charlson Comorbidity Index; CI = confidence interval; admission = admission for TRUS biopsy; Prostate ca. = prostate cancer diagnosed after TRUS biopsy; RR = relative risk; TRUS = transrectal ultrasound-guided.

Table 3
Risk factors for significant bleeding after TRUS biopsies.

Risk factor	Significant bleeding (1.14%)					
	Univariate RR	95% CI	*p*	Multivariate RR	95% CI	*p*
Age	1.02	1.01–1.03	0.015	1.01	0.99–1.03	0.318
Prostate ca.	0.61	0.52–0.83	<0.001	0.67	0.46–0.96	0.028
Admission	2.04	1.43–2.90	<0.001	1.18	0.69–2.02	0.544
CCI ≥2	2.91	1.82–4.63	<0.001	2.65	1.76–3.85	<0.001

Admission = admission for TRUS biopsy; CCI = Charlson Comorbidity Index; CI = confidence interval; admission = admission for TRUS biopsy; Prostate ca. = prostate cancer diagnosed after TRUS biopsy; RR = relative risk; TRUS = transrectal ultrasound-guided.

received at least six dosages of continuous intravenous antibiotics treatment within 7 days after prostate biopsy had an infection that required treatment (Table 4).

Age, diagnosis of prostate cancer, hospitalization, and a CCI value of ≥1 were all significant risk factors for postbiopsy voiding difficulty and severe infection (Tables 2 and 4) in univariate and multivariate analyses. For postbiopsy massive bleeding (Table 3), age and biopsy during admission were significant factors in univariate analysis. Only a diagnosis of cancer and a CCI value of ≥2 were significant in univariate analysis and multivariate analysis, and patients diagnosed with prostate cancer had fewer bleeding complications after biopsy.

4. Discussion

The undertaking of prostate biopsy *via* the transrectal route is the "gold standard" and necessary procedure to diagnose prostate cancer. Biopsy-related mortality and morbidity are important with regard to the high prevalence of prostate cancer in an older male population.[9–12]

Table 4
Risk factors for infection requiring treatment after TRUS biopsies.

Risk factor	Infection requiring treatment (6.59%)					
	Univariate RR	95% CI	*p*	Multivariate RR	95% CI	*p*
Age	1.03	1.02–1.04	<0.001	1.01	1.00–1.02	0.002
Prostate ca.	1.53	1.33–1.76	<0.001	1.03	1.01–1.06	0.025
Admission	2.74	2.20–3.24	<0.001	2.24	1.92–2.60	<0.001
CCI ≥1	2.22	1.63–3.02	<0.001	1.77	1.29–2.43	<0.001

Admission = admission for TRUS biopsy; CCI = Charlson Comorbidity Index; CI = confidence interval; admission = admission for TRUS biopsy; Prostate ca. = prostate cancer diagnosed after TRUS biopsy; RR = relative risk; TRUS = transrectal ultrasound-guided.

Based on the nationwide database of NHI in Taiwan, the postbiopsy sepsis-related mortality rate was 0.13%, which was higher than the Prostate, Lung, Colorectal, and Ovarian Cancer Screening (PLCO) trial rate of 0.095%,[13] but lower than the three-country European Randomized Study of Screening for Prostate Cancer (ERSPC—Finland, The Netherlands, and Sweden) trial rate of 0.24%.[14] However, in the PLCO trial, the 120-day mortality of the nonbiopsy group was 0.18%, and the multivariate relative risk of biopsy in excess of the control group was not statistically significant [$p = 0.49$, 95% confidence interval (CI) = 0.2–1.1].[13] The data results in our study lies in between the results of the other two studies, which implies that the postbiopsy sepsis rate would not lead to a greater mortality in Taiwan than in other countries. In additon, the ERSPC (Finland, The Netherlands, and Sweden) study[14] and PLCO study[13] indicate no greater mortality rate after a TRUS biopsy. The Rotterdam section of ERSPC trial even showed reduced prostate cancer mortality in a previous study,[15] and a corrective study.[16] Therefore, the mortality rate after TRUS biopsy is apparently minimal and not significantly higher, and the TRUS biopsy may also reduce mortality of individuals who are further diagnosed with prostate cancer.

In our study, the prostate cancer diagnosis rate was 36%, which is much higher than the rate in the ERSPC Rotterdam section (biopsy, 12.8%; nonbiopsy, 6.6%; total, 9.7%)[16] and the Surveillance Epidemiology and End Result study (SEER; 17.1%).[17] However, it is only slightly higher than the rate in the PLCO trial (biopsy, 32.3%).[13] However, in an Ontario, Canada study,[7] the prostate cancer diagnosis rate was even higher at 44.6%. The mean age in each group was 62.4 years in the ERSPC trial and 63.7 years in the PLCO trial—both ages were younger than in our current study. Another single institutional study in Taiwan revealed that the prostate cancer diagnosis rate was 23.58% and the individuals' mean age was 67.3 years.[18] Therefore, we believe that in Taiwan, TRUS prostate biopsy is performed in an older population with a higher cancer detection rate.

We were able to study three major complications after TRUS prostate biopsies—voiding difficulty, significant bleeding, and infection that required treatment. The rates of these complications were 9.76%, 1.14%, and 6.59%, respectively. Among the three major complications, infection requiring treatment accounted for most post-TRUS biopsy readmissions because voiding difficulty could be managed by catheterization in an ambulatory clinic or in an emergency room. Significant bleeding has a smaller occurrence rate. The SEER study indicates that the 30-day hospitalization rate is 6.9%, which is similar to the rate of 6.59% in our study for infection that required treatment.[17] By contrast, the infection complication and hospital admission rates in the Rotterdam section of the ERSPC were 4.2% and 0.8%, respectively.[6] However, in the Ontario study, the 30-day hospital admission rate was 1.4% for all patients.[7] For patients with prostate cancer, the admission rate was 0.8% (which increased from

0.4% in 1996 to 0.9% in 2005); for patients without prostate cancer, the admission rate was 1.9% (which increased from 1.0% in 1996 to 4.1% in 2005).[7] The complication rate trend is increasing, although it is still lower than the rate in the SEER trial, the Rotterdam section of ERSPC, and our study. Therefore, there are concerns that performing more unnecessary biopsies may result in more complications, especially for men without prostate cancer in Canada.

In a single institutional study in Taiwan in 2007,[18] the rate of acute urinary retention was 2.1%, which is lower than the rate in our study at 9.76%; the rate of hematuria plus rectal bleeding was 1.9 ± 0.2%, which was higher than our significant bleeding rate of 1.14%; and the rate of infection-related complications such as acute prostatitis, epididymitis, and sepsis was 3.8%, 0.2%, and 0.05%, respectively, which was apparently lower than our rate of 6.59% for infections requiring treatment.[18] In our study, the increased urinary retention rate and infection requiring treatment may be the result of having data associated with a higher average age of the patients. The difference between our study and the single institutional study may be attributable to having dissimilar targeted populations, different definitions of complications, and altered methodological approaches.

In earlier studies, Chiang et al[18] report that only an enlarged prostate was an associated risk factor for acute prostatitis and urinary retention. Loeb et al[17] report that later year, nonwhite ethnicity, and higher comorbidity scores were significantly associated with an increased risk of infection-related complications in the SEER study, and prostate enlargement and diabetes were significant risk factors for fever after TRUS biopsy in the Rotterdam section of the ERSPC trial.[6] Pinsky et al[13] suggest that prostate enlargement or inflammation is significantly associated with a higher rate of infectious and noninfectious complications, whereas black ethnicity was associated with infectious complications and repeated biopsy with noninfectious complications. In summary, an enlarged prostate, nonwhite ethnicity, and comorbidities such as diabetes are associated risk factors for complications after TRUS biopsy in the literature. Our study revealed that age, diagnosis of cancer, a CCI value of $\geq$1, and biopsy during admission were the statistically significant risk factors of postbiopsy voiding difficulty and infection episodes, whereas a diagnosis of cancer and a CCI value of $\geq$2 were associated with significant bleeding after a TRUS biopsy.

In conclusion, we studied TRUS prostate biopsy by focusing on associated complications using a nationwide research database. The most frequently encountered complication of prostate biopsy was postbiopsy voiding difficulty, followed by infection requiring treatment, and significant bleeding. Approximately one in three patients who received TRUS biopsy has been diagnosed with prostate cancer in Taiwan. Age, diagnosis of cancer, CCI value $\geq$ 1, and undergoing a biopsy as an inpatient procedure were significant risk factors of postbiopsy voiding difficulty and infection episodes; a CCI value $\geq$ 2 was correlated with significant bleeding after TRUS biopsy, whereas diagnosis of cancer was inversely correlated. The sepsis-related mortality rate was 0.13%.

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