Emergency attendances and hospitalisations for complications after transrectal ultrasound-guided prostate biopsies: a five-year retrospective multicentre study

KC Cheng *, WC Lam, HC Chan, CC Ngo, MH Cheung, HS So, KM Lam

ABSTRACT

Introduction: Transrectal ultrasound-guided (TRUS) prostate biopsy is an established procedure for diagnosis of prostate cancer. Complications after TRUS biopsy are not well reported in Hong Kong. This study evaluated the 5-year incidences of TRUS biopsy complications and potential risk factors for those complications.

Methods: This was a retrospective review of biopsies performed from 2013 to 2017 in two local hospitals, using data retrieved from electronic medical records. The primary outcome was the occurrence of complications requiring either emergency attendances or hospitalisations within 30 days after biopsy. Potential risk factors were examined using multiple logistic regression analysis.

Results: In total, 1699 men were included (mean age ± standard deviation: 67 ± 7 years; median prostate-specific antigen level: 7.9 µg/L [interquartile range, 5.5-12.6 µg/L]); 4.3% had pre-biopsy bacteriuria. Overall, 5.7% and 3.8% of post-biopsy complications required emergency attendances and hospitalisations, respectively. Gross haematuria and rectal bleeding requiring emergency attendances developed in 2.1% and 0.4% of men; 0.8% and 0.4% required hospitalisations. Furthermore, 1.5% of men developed acute urinary retention requiring hospitalisations; 1.9% and 1.2% had post-biopsy infections requiring emergency attendances and hospitalisations, respectively, and 0.9% had urosepsis requiring hospitalisations. Prostate volume >48 cc was associated with an increased risk of post-biopsy retention (odds ratio 2.75, 95% confidence interval: 1.23-4.17).

Conclusions: The rate of overall complications after TRUS biopsy was low. The most common complications requiring emergency attendances and hospitalisations were gross haematuria and acute urinary retention, respectively. Prostate volume >48 cc increased the risk of post-biopsy urinary retention.

New knowledge added by this study
- Complications requiring emergency attendances or hospitalisations after transrectal ultrasound-guided (TRUS) prostate biopsies are uncommon.
- The most common complications requiring emergency attendances and hospitalisations are gross haematuria and acute urinary retention, respectively.
- The presence of a large prostate (volume >48 cc) increases the risk of acute urinary retention after TRUS biopsy. However, no specific factors are associated with increased risk of post-biopsy infections.

Implications for clinical practice or policy
- Patients with large prostate should be counselled for the increased risk of urinary retention after TRUS biopsy.
- Despite the presence of antibiotic-resistant bacteria in urine and blood cultures, patients who develop sepsis after TRUS biopsy are likely to recover after a brief period of hospitalisation.

Introduction
Transrectal ultrasound-guided (TRUS) prostate biopsy, introduced in 1989,1 is an established and longstanding procedure for detection of prostate cancer. Because it can be learned rapidly and comprises a simple, office-based procedure, TRUS biopsy remains the most commonly performed procedure for diagnosis of prostate cancer.2,3
經直腸前列腺穿刺活組織檢查併發症：五年期多中心回顧性調查

鄭冠中、林穎聰、陳開澤、敖章鐘、張文虹、蘇慶成、林建文

引言：經直腸前列腺穿刺活組織檢查是診斷前列腺癌的有效方法。不過，在香港有關檢查引起併發症的具體資料並不多。本研究審視香港兩間醫院五年內發生的活檢後併發症，並嘗試找出引起併發症的風險因素。

方法：這項回顧性研究審視由2013年至2017年在兩間公立醫院所做的活檢，主要研究結果包括活檢後30天內的急症求診率及住院率。研究利用多元邏輯斯迴歸分析檢視潛在的併發症風險因素。

結果：1699名男性被納入研究，平均年齡67歲（標準差：7歲），前列腺特異抗原指數的中位數為7.9 µg/L（四分位距：5.5-12.6 µg/L），當中4.3%患者活檢前小便帶菌。30天內急症求診率和住院率分別為5.7%及0.9%，因感染到急症室求診的患者佔4.3%及0.4%，分別有0.8%及0.4%患者須住院。急性尿瀦留患者佔1.5%，全部須住院。因活檢後感染到急症室求診的患者佔1.9%，須住院的佔1.2%。因感染引致敗血症的住院率為0.9%，前列腺體積超過48 cc的患者在活檢後引發尿瀦留的機會較高（比值比：2.75，置信區間：1.23-4.17）。

結論：經直腸前列腺穿刺組織檢查的併發症低。最常見因併發症往急症室求診及住院的分別是血尿及尿瀦留。前列腺體積超過48 cc的患者在活檢後引發尿瀦留的機會較高。

However, TRUS biopsy is associated with significant risks. Instances of bleeding are common, including haematuria, rectal bleeding, and haemospermia; however, these are generally mild and self-limiting. The most worrisome complication is post-biopsy infection, which occurs in 0% to 6.3% of men after TRUS biopsy. The risk is low, but the consequences are serious in affected patients. There is recent evidence to suggest that increasing numbers of quinolone-resistant organisms are contributing to the development of post-biopsy sepsis.

In Hong Kong, there have been few reports of TRUS biopsy complications. Some studies have focused on infective complications in relatively small numbers of patients. Therefore, we reviewed TRUS biopsy performed over a 5-year period in two local hospitals to evaluate the incidences and types of complications, as well as their associated risk factors. This could provide an important insight into the overall TRUS biopsy complications, including infective and non-infective complications in the local population.

Methods

Patients and study design

This retrospective cohort analysis included men who underwent TRUS biopsy procedures during the period from 2013 to 2017 in United Christian Hospital, Hong Kong and Tseung Kwan O Hospital, Hong Kong. All patients who underwent TRUS biopsy procedures were included in the analysis.

Biopsy procedure

All biopsies were performed as day procedures. A 7.5-MHz biplanar transrectal ultrasound probe and 18-gauge needles with side-firing needle-guides were used for biopsy. Each patient was positioned in the left lateral posture with both hips and knees flexed. Prostate size measurement was calculated using the ellipsoidal formula. Topical lidocaine jelly and local anaesthetic injection with 10 mL of 1% plain lidocaine were used routinely in one hospital; these were injected into the area between the prostatic base and seminal vesicles. The other hospital used topical lidocaine alone. Six-core to 12-core systemic biopsies were performed depending on the hospital involved and the time frame of the biopsy procedure, as the two centres have changed the practice in performing more number of cores with time. Each patient was discharged on the same day after completion of the procedure. Clinical follow-up was performed at 4 weeks post-biopsy in an out-patient clinic to review the pathology findings.

Follow-up assessment

Patients who were admitted for biopsies were identified using the Clinical Data Analysis and Reporting System. Clinical records (ie, discharge summary, emergency case notes, clinical consultation notes, laboratory results, and ultrasound findings) were retrieved using the hospital-based Clinical Management System and the territory-wide
Electronic Patient Record, which comprises a centralised medical records system shared by all public hospitals. Thus, men who had been admitted to another public hospital for complications could be identified. The patients’ records were examined and the occurrence of complications was determined using a standardised form. During post-biopsy follow-up examinations, clinical records from the Clinical Management System were examined to identify any potential attendances or admissions to private sector hospitals owing to complications. The primary outcome in this study was the occurrence of complications within 30 days after biopsy. Complications were defined as events requiring either emergency attendances or hospitalisations; these events were analysed separately. Post-biopsy urinary tract infections (PBI) were defined as the presence of urinary tract infection symptoms (dysuria, with or without frequency, urgency, or suprapubic pain) after biopsy, with or without sepsis. Based on the Sepsis-3 criteria, sepsis was defined as an acute increase in the Sequential Organ Failure Assessment score of ≥2. Acute urinary retention (AUR) was defined as acute painful retention of urine requiring catheterisation. Any lower urinary tract symptoms (LUTS) that occurred or worsened after biopsy, which required emergency attendances, were also recorded.

Statistical analysis
Statistical calculations were computed with the SPSS (Windows version 22.0; IBM Corp, Armonk [NY], United States). For examination of potential risk factors, continuous variables, such as PSA level and prostate size, were categorised based on the median values. The Chi squared test was used to compare complications between the two hospitals. Multiple logistic regression models were used to investigate potential risk factors for complications.

Results
In total, 1710 men were admitted to either of the two hospitals for TRUS biopsy procedures during the study period. Eleven men were excluded because they refused to undergo TRUS biopsy after admission; therefore, 1699 men were included in the study. The mean age (± standard deviation) of the men was 67 ± 7 years and median PSA level was 7.9 µg/L (interquartile range, 5.5-12.6 µg/L). Of the 1699 men in the study, 310 (18.2%) had a suspicious digital rectal examination of the prostate; the overall cancer detection rate was 19.8%. Characteristics and results of the biopsies are shown in Table 1. Overall, 5.7% and 3.8% of post-biopsy complications required emergency attendances and hospitalisations, respectively (Table 2). There were no occurrences of mortality in the entire cohort.
Bleeding complications
Overall, 2.1% of men in the study developed gross haematuria requiring emergency attendances, and 0.8% were hospitalised for further management. Haematuria subsided with conservative treatment in all affected men; no transfusions or emergency surgical interventions were needed. Rectal bleeding occurred in 0.4% of men; all required hospitalisations. Rectal bleeding resolved spontaneously in all affected men, except two who required rectal packing with adrenaline gauze for haemostasis. There were no cases of haemospermia requiring emergency attendances. No risk factors could be identified for emergency attendances or hospitalisations related to any bleeding complications (Table 3). Importantly, the continuation of low-dose aspirin was not associated with an increased rate of bleeding complications.

Retention of urine and lower urinary tract symptoms
In all, 1.5% of men in the study developed AUR; all required hospitalisations. During these hospitalisations, the men were assessed by voiding trials; all were able to void spontaneously within 2 to 3 days. Acute-onset LUTS was present in 0.4% of men who had emergency attendances, and 0.1% of the men required hospitalisation. Prostate size >48 cc was associated with a nearly 3-fold increase in the risk of post-biopsy retention (odds ratio=2.75, 95% confidence interval: 1.23-4.17; Table 3). No risk factors were identified with respect to the occurrence of LUTS.

Post-biopsy infection
Pre-biopsy bacteriuria was present in 4.3% of men in this study. The most common causative bacterial species was *Escherichia coli* (1.8%) [Table 4]. Emergency attendances and hospitalisation rates for PBI were 1.9% and 1.2%, respectively. Sepsis occurred in 0.9% of men in this study, all of whom required hospitalisations (Table 2). Among patients who developed sepsis, none had a positive pre-biopsy urine culture. Post-sepsis urine cultures were positive in 46.7% (7/15) of the men who developed sepsis; all of these positive cultures showed growth of *E. coli*, and 57% (4/7) of the cultures demonstrated quinolone resistance. Blood cultures were positive in

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**TABLE 2. Complications requiring emergency attendances or hospitalisations after prostate biopsies (n=1699)**

<table>
<thead>
<tr>
<th></th>
<th>Emergency attendances</th>
<th>Hospitalisations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>96 (5.7%)</td>
<td>65 (3.8%)</td>
</tr>
<tr>
<td>Infective complications</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall PBI</td>
<td>32 (1.9%)</td>
<td>20 (1.2%)</td>
</tr>
<tr>
<td>Sepsis</td>
<td>15 (0.9%)</td>
<td>15 (0.9%)</td>
</tr>
<tr>
<td>Non-infective complications</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Haematuria</td>
<td>35 (2.1%)</td>
<td>14 (0.8%)</td>
</tr>
<tr>
<td>Rectal bleeding</td>
<td>6 (0.4%)</td>
<td>6 (0.4%)</td>
</tr>
<tr>
<td>Haemospermia</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>AUR</td>
<td>25 (1.5%)</td>
<td>25 (1.5%)</td>
</tr>
<tr>
<td>LUTS</td>
<td>7 (0.4%)</td>
<td>2 (0.1%)</td>
</tr>
</tbody>
</table>

Abbreviations: AUR = acute urinary retention; LUTS = lower urinary tract symptoms; PBI = post-biopsy infection
* Data are shown as No. (%)

**TABLE 3. Multiple logistic regression model examining risk factors for non-infective complications**

<table>
<thead>
<tr>
<th></th>
<th>Haematuria</th>
<th>Hospitalisation</th>
<th>AUR</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Emergency Attendance</td>
<td>OR (95% CI)</td>
<td>P value</td>
</tr>
<tr>
<td>Age</td>
<td>0.17</td>
<td>0.96 (0.91-1.01)</td>
<td>0.68</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>0.24</td>
<td>1.22 (0.93-1.45)</td>
<td>0.46</td>
</tr>
<tr>
<td>PSA ≥8</td>
<td>0.87</td>
<td>0.94 (0.43-2.03)</td>
<td>0.62</td>
</tr>
<tr>
<td>Prostate size &gt;48 cc</td>
<td>0.68</td>
<td>1.18 (0.54-2.57)</td>
<td>0.84</td>
</tr>
<tr>
<td>Pre-biopsy bacteriuria (treated)</td>
<td>0.78</td>
<td>1.23 (0.30-5.07)</td>
<td>0.16</td>
</tr>
<tr>
<td>Low-dose aspirin</td>
<td>0.54</td>
<td>1.24 (0.78-1.45)</td>
<td>0.34</td>
</tr>
<tr>
<td>Periprostatic nerve block</td>
<td>0.16</td>
<td>0.34 (0.08-1.53)</td>
<td>0.12</td>
</tr>
<tr>
<td>No. of cores ≥10</td>
<td>0.56</td>
<td>1.57 (0.35-7.01)</td>
<td>0.31</td>
</tr>
<tr>
<td>Repeated biopsies</td>
<td>0.62</td>
<td>0.82 (0.36-1.84)</td>
<td>0.46</td>
</tr>
<tr>
<td>Prostate cancer</td>
<td>0.25</td>
<td>2.09 (0.59-7.38)</td>
<td>0.66</td>
</tr>
</tbody>
</table>

Abbreviations: AUR = acute urinary retention; CI = confidence interval; OR = odds ratio; PSA = prostate-specific antigen
40% (6/15) of the men who developed sepsis; all of these positive cultures showed growth of *E. coli*, and 83% (5/6) of the cultures demonstrated quinolone resistance. None of the men required intensive care and none developed prostate abscesses. The median hospital stay for men with sepsis was 6 days (interquartile range, 4–10 days).

Treatment for bacteriuria and the presence of diabetes mellitus both showed no associations with overall infection or urosepsis. No other factors tested including age and prostate size were associated with infective complications. There were no differences in the rates of overall complications requiring either emergency attendances (6.5% vs 4.6%, *P*=0.10) or hospitalisations (3.9% vs 3.8%, *P*=0.95) between the two hospitals. Moreover, there were no differences in the rates of overall post-biopsy infection or sepsis (0.8% vs 1.6%, *P*=0.13 and 0.5% vs 1.4%, *P*=0.19).

**Discussion**

**Non-infective complications**

Non-infective complications after TRUS biopsy were common in this study; fortunately, most comprised minor complications that did not require additional treatment. Using questionnaires and telephone for follow-up of patients who underwent TRUS biopsy, the ProtecT Study group found that haematuria occurred in 65.8%, rectal bleeding occurred in 36.8%, and haemospermia occurred in 92.6%, within 35 days after biopsy. A recent systematic review of TRUS biopsy complications reported wider ranges of complication rates: haematuria in 27.9% to 64.5% of patients, haemospermia in 6% to 90.1% of patients, and rectal bleeding in 11.5% to 40% of patients. These wide ranges of complication rates were largely dependent on the methods by which the complications were registered. In our study, the reported bleeding rate was lower, as we only included patients with complications requiring emergency attendances. The differences in our findings suggest that post-biopsy bleeding might generally be mild; thus, it does not require medical consultation.

Prostate size is reportedly associated with the risk of haematuria after biopsies, as is the number of cores, although this particular point remains controversial. However, our study did not find evidence to support these relationships. The post-biopsy retention rate in our study was comparable with that in the literature (0.2%–1.7%). All men had successful voiding trials in our cohort and did not require surgical intervention. Importantly, we found that prostate size was a risk factor for post-biopsy retention, consistent with the results of two other studies.

**Infective complications**

Infective complications requiring hospitalisation have been reported in 0% to 6.3% of patients after TRUS biopsy. The Global Prevalence Study of Infections in Urology 2013 revealed post-biopsy infection in 5.2% of patients; of them, 3% required hospitalisation. A recently published population-based study showed an increasing trend in infective complications, comprising a four-fold increase in overall hospitalisations over 10 years. In the present study, we could not perform any temporal analyses of complications because the length of the study was insufficient; to the best of our knowledge, there have been no such temporal analyses in Hong Kong. The infection rate in our cohort was comparatively lower than that of most international studies, and similar to that in prior studies elsewhere in Asia (0% and 0.5% of PBI), as well as in Hong Kong (0.5% and 3.9%). Reasons for the apparent lower infection rate in people of Asian ethnicity compared with those of other ethnicities are unclear. Tsu et al reported that patients who underwent TRUS biopsy exhibited a high prevalence (53.6%) of antibiotic-resistant flora in the rectum, although the PBI rate remained low among these patients (2.4%). Numerous risk factors have been associated with the development of PBI. However, in the present study, we did not identify any factors that could predict the risk of PBI.

A positive urine culture was not a mandatory requirement to define PBI in this study, as a significant proportion of men who had urinary tract infection symptoms without systemic inflammatory response syndrome were treated and discharged directly from the emergency department, and most did not provide urine cultures. Thus, the emergency case notes were reviewed to determine whether PBI had occurred. In contrast, for men who had been hospitalised with sepsis, urine and blood cultures were available for analysis.

There were no reports of mortality in our cohort. In general, death directly related to biopsy is exceedingly rare and most patients die because of other factors. The reported mortality rates after TRUS biopsy are 0.09% to 1.3%, depending on the length of the post-biopsy follow-up period. Data from a prostate cancer screening trial showed a mortality rate of 0.095% in biopsy patients, which was

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**TABLE 4. Types of pre-biopsy bacteriuria**

<table>
<thead>
<tr>
<th>Bacteria</th>
<th>No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Citrobacter species</em></td>
<td>5 (0.3%)</td>
</tr>
<tr>
<td><em>Escherichia coli</em></td>
<td>30 (1.8%)</td>
</tr>
<tr>
<td><em>Enterococcus species</em></td>
<td>8 (0.5%)</td>
</tr>
<tr>
<td><em>Klebsiella pneumoniae</em></td>
<td>9 (0.5%)</td>
</tr>
<tr>
<td><em>Proteus mirabilis</em></td>
<td>15 (0.9%)</td>
</tr>
<tr>
<td><em>Pseudomonas aeruginosa</em></td>
<td>5 (0.3%)</td>
</tr>
</tbody>
</table>

* Data are shown as No. (%)
and education are needed for patients with a large

Transperineal or transrectal approaches
There has been a recent surge of interest, both
in Hong Kong and internationally, in performing
transperineal prostate biopsies. Transperineal
biopsies are advantageous in that they have an
extremely low risk of sepsis and enable improved
sampling of tumours in the anterior prostate. In
transperineal biopsy, the needle is passed through
clean and prepared skin, rather than faeces or bowel;
this method is presumed to eliminate post-biopsy
infection. In 2013, a large systematic review of
transperineal biopsy showed no instances of sepsis,
with only a few reported cases of PBI (0%-1.6%).
Transrectal biopsy exhibits difficulty in sampling
the anterior prostate. Indeed, transperineal biopsy
reportedly exhibits a superior cancer detection
rate, especially in terms of tumours in the anterior
prostate.

Despite these advantages in the rate of post-
bio

biopsy sepsis and sampling of anterior tumours,
the transperineal approach has limitations. These
include longer operating time, greater procedure-
related pain, and increased post-biopsy retention,
particularly in relation to the use of template mapping
protocols. A systematic review and meta-analysis
conducted in 2012, which compared the outcomes of
transperineal and transrectal biopsies, did not show
any differences in rates of complications between
the two approaches. In our opinion, additional
studies are needed to compare the two approaches
in terms of cancer detection rate, complications,
cost-effectiveness, and patient-reported outcomes
before wide adoption of the transperineal approach
is recommended.

In early 2018, we began exploratory use of
transperineal prostate biopsy; thus far, we have
used it for assessment of 71 patients. None of the
patients have shown signs of sepsis or urinary
tract infections; two patients were readmitted after
biopsy for urethral bleeding and three patients
were readmitted for urinary retention. The number
of biopsies performed thus far is insufficient for a
meaningful comparison with existing data from
transrectal biopsies.

Limitations and future studies

To the best of our knowledge, this is the first study in
Hong Kong to provide data regarding non-infective
complications of TRUS biopsy. It provides valuable
information for patients and can be used by clinicians
during treatment counselling. Special precautions
and education are needed for patients with a large
prostate, as they exhibit an increased risk of post-
bio

biopsy retention. Nonetheless, the value of this study
was limited by its retrospective nature.

The complications recorded were based solely
on emergency attendances and hospitalisations in
all public hospitals; importantly, attendances to
private sector hospitals might have been missed.
However, because approximately 90% of in-patient
care in Hong Kong is provided by public hospitals,
we presume that our approach enabled us to retrieve
data regarding the vast majority of post-biopsy
complications that required hospitalisations.
In addition, patients who had attended private
hospitals for complications, then attended public
out-patient clinics for follow-up, could be identified
and recorded unless they also selected private clinic
follow-up.

Milder complications which did not require
emergency attendances or hospitalisations, as
well as sexual dysfunction and post-biopsy pain,
could not be assessed in this study. Because of its
retrospective design, we also could not report on
prior antibiotics exposure and travel history among
the patients, which limits analyses of risk factors.

Approximately 20% of men in the

cohort had sextant biopsies. The use of this lower
number of cores might have led to underestimation
of the rate of complications, compared with current
standards for biopsy, in which 10 to 12 cores are
taken.

Finally, a locoregional prospective multicentre
study with other Asian nations would provide
valuable insights into complications after prostate
biopsies in the Asian population; it would also aid
in assessments of differences in complications
compared with Western nations.

Conclusions

Complications requiring emergency attendances
or hospitalisations after transrectal prostate biopsy
were uncommon; the most common complications
requiring emergency attendances and hospitalisations
were gross haematuria and AUR, respectively. Prostate
volume >48 cc was a risk factor for post-biopsy urinary
retention, but no specific risk factors were identified
for post-biopsy infections. Patients with large prostate
should be counselled for the increased risk of urinary
retention after TRUS biopsy.

Author contributions

All authors had full access to the data, contributed to the
study, approved the final version for publication, and take
responsibility for its accuracy and integrity.

Concept or design: KC Cheng, KM Lam.
 Acquisition of data: KC Cheng, WC Lam, KM Lam.
 Analysis or interpretation of data: KC Cheng.
Drafting of the article: KC Cheng.
Critical revision for important intellectual content: HC Chan,
CC Ngo, MH Cheung, HS So.

Declaration
This research has been presented in part at the 15th Urological
Association of Asia Congress 2017, 4-6 August 2017, Hong
Kong.

Conflicts of interest
All authors have disclosed no conflicts of interest.

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Ethics approval
This study was approved by the Kowloon Central/Kowloon
East Research Ethics Committee (Ref KC/KE-19-0182/ER-1).

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system in Hong Kong and its referential significance to