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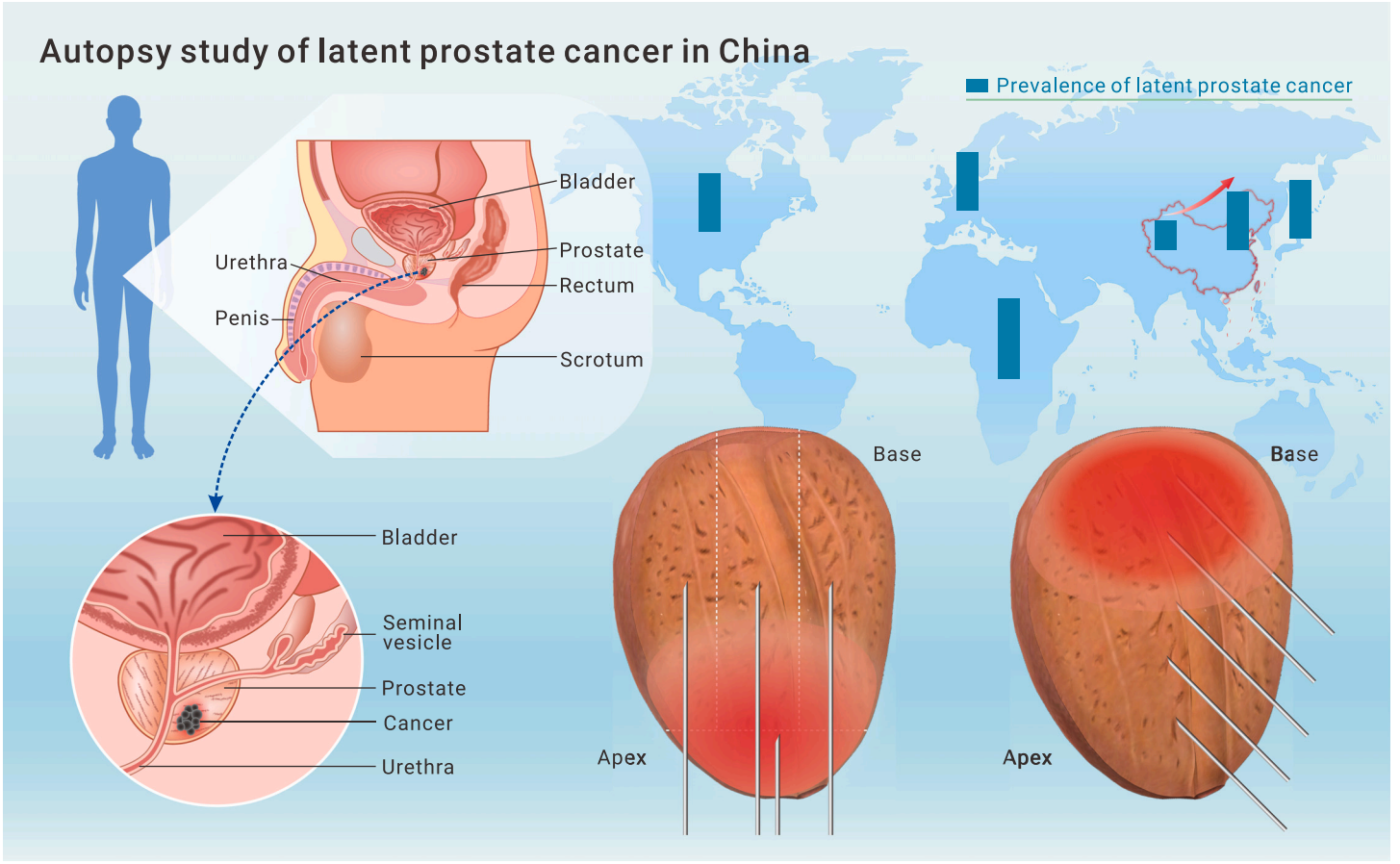
GRAPHICAL ABSTRACT



PUBLIC SUMMARY

- We conducted prostate autopsies to investigate latent cancer epidemiology and measure the accuracy of prostate biopsy.
- In recent decades, the prevalence of latent prostate cancer has increased in China.
- Transperineal and transrectal biopsies exhibited similar sensitivities but different preferential areas.
- Both methods of biopsy missed one-third of cases with large lesions, most of which were in the anterior prostate.

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Prostate cancer detected by autopsy is named latent prostate cancer. As the repertoire of clinical prostate cancer, latent cancer may better reflect the disease burden. Unlike clinical prostate specimens, which are obtained exclusively from biopsy-positive cases, prostate specimens obtained through autopsy provide information on biopsy-negative cases, helping calculate the true sensitivity of prostate biopsy. From 2014 to 2021, we collected autopsy specimens of the prostate from body donors in China and performed transperineal and transrectal biopsies on specimens before step-sectioning and pathological measurements. We found that the crude prevalence of latent prostate cancer in middle-aged and elderly men was 35.1% (81/231), which was higher than previous estimates for Chinese populations. The overall per-patient sensitivities of transperineal and transrectal biopsies were not significantly different (33.3% vs. 32.1%, p = 0.82), but the two approaches differed in preferential sampling area along the proximal-distal axis of the prostate. Transperineal biopsy had a higher sensitivity for detecting clinically significant lesions in the distal third (34.7% vs. 16.3%, p = 0.02) and distal half (30.6% vs. 18.1%, p = 0.04), while transrectal biopsy had a higher sensitivity for lesions in the proximal half (25.0% vs. 13.9%, p = 0.046). Both transperineal and transrectal methods of biopsy missed most small lesions (<0.1 mL) and 35.3% (6/17) of large lesions (>0.5 mL). In conclusion, the prevalence of latent prostate cancer in China has increased over the past 2 decades. Systematic transperineal and transrectal methods of biopsy had comparable sensitivities but had different preferential sampling areas. Both approaches miss one-third of large lesions.

INTRODUCTION

Prostate cancer is one of the most common malignancies among men.[1] However, most patients with prostate cancer remain asymptomatic and undiagnosed throughout their life.[2] Prostate cancer that is not diagnosed before death and is only found at autopsy is named latent prostate cancer. Data from these subclinical cases are indispensable to expand our understanding of prostate cancer.

The prevalence of clinically diagnosed prostate cancer is largely affected by diagnostic and therapeutic approaches. On the other hand, latent prostate cancer, as the repertoire of clinical prostate cancer, can better reflect the disease burden. The prevalence of latent prostate cancer in Asian populations has long been considered much lower than that in African and European populations.[3,4] Previous autopsy studies in Chinese populations also reported similar results,[2,5,6] but studies over the past 20 years are lacking. In our previous study comprising 113 prostate autopsies, we found a higher prevalence of latent prostate cancer than expected.[7] Here, we expanded our sample size to provide an updated and comprehensive picture of the latent prostate cancer status in China.

Specimens obtained through radical prostatectomy are used as a gold standard to evaluate the accuracy of prostate biopsy.[8–11] In clinical cohorts, patients with false-negative biopsies or those who have not undergone surgery do not have whole-mount pathology. This unavoidable selection bias limits the understanding of biopsy-missed prostate cancer lesions, making it difficult to plan for repeat biopsy or improve the biopsy scheme.

A prostate biopsy can be performed through the transperineal (TP) or transrectal (TR) approach.[12] It is still controversial which of these methods is superior regarding diagnostic accuracy as the initial method of biopsy.[13–17] Previous studies used the detection rate as a surrogate endpoint, which limited the reliability of their results.

TP biopsy was reported to provide enough sample of the anterior[18–21] and apical areas[21,22] of the prostate, allowing more accurate staging than TR biopsy.[20,21,23] These findings necessitate further confirmation in a head-to-head comparison study using whole-mount pathology as the gold standard.

Whole-mount pathology of biopsy-negative patients is needed to address these clinical concerns. Biopsy simulation on prostate autopsy specimens helps design such studies. Previous studies have attempted to assess the true sensitivity of prostate biopsy. Haas et al. simulated TR biopsy on prostate autopsy specimens to assess the diagnostic ability of 6-, 12-, 18-, and 36-core biopsy.[24,25] Crawford et al. used computer models of autopsy prostates to simulate and measure TP biopsy.[26] Rocco et al. performed TP biopsy on patients before radical cystoprostatectomy to obtain whole-mount pathology from biopsy-negative patients.[27] So far, no study has evaluated the diagnostic accuracy of TP and TR biopsy methods in a head-to-head study.

In this autopsy study, we investigated the epidemiology of latent prostate cancer in China. Furthermore, we conducted TP and TR systematic 12-core biopsies on autopsy prostates to compare the sensitivities of the two approaches in a head-to-head study. We also reported the characteristics of the lesions that were detected and undetected.

MATERIALS AND METHODS

Study design

From 2014 to 2021, we prospectively and consecutively collected prostate specimens from postmortem donors. Male decedents who died of causes other than prostate cancer and had no history of prostate cancer were included. The exclusion criteria were as follows: (1) the presence of glandular defects and (2) loss of one or both seminal vesicle glands. The enrollment and exclusion of specimens are shown in Figure 1. Reporting of the results followed STARD (Standards for the Reporting of Diagnostic Accuracy Studies) practice.

This study was registered in the Chinese Clinical Trial Registry (https://www.chictr.org.cn) (Registration number: ChiCTR1900027752) and was approved by the Ethics Review Committee of Peking Union Medical College Hospital, Chinese Academy of Medical Sciences (ZS-1546).

Of 261 registered donors, three were excluded because they had clinically diagnosed prostate cancer, and 26 were excluded because of incomplete glands. In total, 119 patients randomly underwent transperineal biopsy first, and 113 participants randomly underwent transrectal biopsy first, with one exception because of missing specimens. In total, 231 patients were included in the final analysis.

Prostate biopsy protocol

All prostate specimens were fixed in 10% formalin for at least 48 h before processing. Surgical forceps were used to hold the glands in a fixed position on the operating table for biopsy simulation. An 8-F catheter was inserted through the urethra to mark the relative position of the urethra and the gland. Two urologists with more than 10 years of experience in prostate biopsy conducted 12-core TP and 12-core TR biopsies on each specimen using 18-gauge, 18-mm-depth Bard biopsy guns (C.R. Bard, Covington, GA, USA). For transperineal biopsy, the needle was inserted parallel to the urethra, mimicking the position used in clinical practice (Figure 2A). For transrectal biopsy, the needle was inserted at an angle of approximately 45° from the posterior surface of the prostate (Figure 2B). The basal end of each

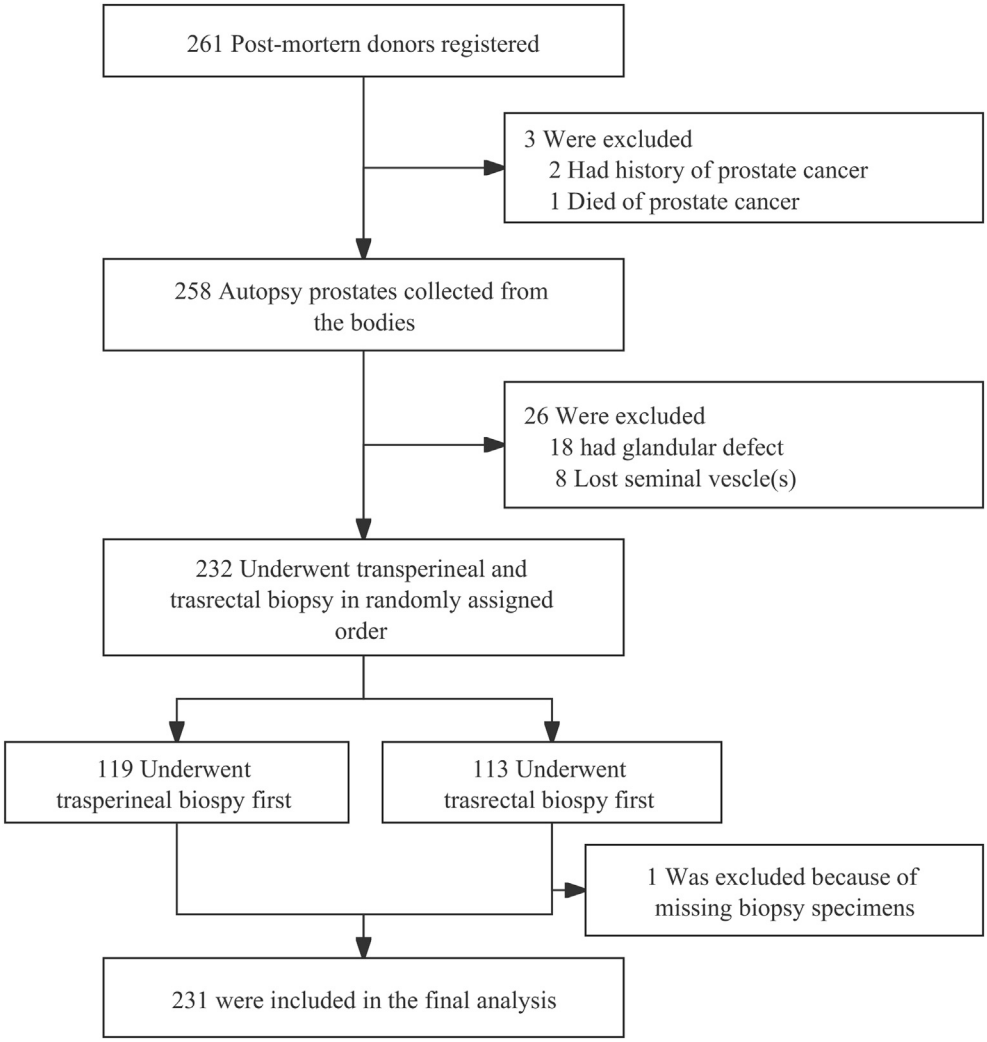


Figure 1. Enrollment of the specimens

core was dyed blue to label the orientation. The target area, depth, and angle of the biopsy needle were determined by the shape of the prostate and the location of the urethra to better simulate *in vivo* ultrasound-guided biopsy. The order in which TP and TR biopsies were performed on each prostate was randomly determined by tossing a coin.

Specimen handling

After the biopsies, excess tissue was removed from the prostate (Figure 2C). The anterior-posterior (AP), left-right (LR), and superior-inferior (SI) diameters of each prostate were measured to estimate the volume of the prostate (PV = $\pi \times$ AP $\times$ LR $\times$ SI/6).[28] A step-sectioning of each autopsy prostate was conducted. The distal 5 mm (apex) was coned and sagittally sliced (2-mm interval). The rest was then transversely sliced (3-mm interval). The proximal 5–10 mm (base) of the prostate was left to be sagittally sliced (2-mm interval). Histologic slices were produced from the biopsy cores and whole-mount prostate sections. The slices were then stained with hematoxylin and eosin for routine histological measurements.

Pathological assessment

Two urological pathologists in our institution with at least 15 years of experience and blinded to samples confirmed the pathological diagnosis. The grade group (GrG) of prostate cancer was assessed following the 2014 ISUP Consensus on Gleason Grading of Prostatic Carcinoma.[29] P504S and CK34βE immunohistochemical staining was performed for cases with difficult diagnosis. A consensus was reached through discussion for any discrepancies in pathological results. All slices from the positive cases were scanned by a Nanozoomer slice scanner (S360, Hamamatsu, Japan) to produce digital slices. The area of the lesion was outlined and automatically calculated using NDP.view2 software (U12388-01, Hamamatsu, Japan) (Figure 2D). Two lesions were considered one if they were on the same slice with a distance smaller than 3 mm or on adjacent levels with an overlapping projection.[30] Cancer volume was calculated by multiplying the section thickness by the area of the lesion. In addition, a correction factor of 1.5 was multiplied for tissue shrinkage.[31]

Index tumor volume (ITV) was defined as the volume of the lesion with the highest GrG in a prostate. If multiple lesions had the same GrG, the ITV was the volume of the largest lesion.[32] We defined clinically significant prostate cancer (csPCa) as prostate cancer with GrG $\geq$2.[33]

Zoning the prostate

The anterior prostate was defined as the area anterior to the coronal plane across the urethra. The peripheral zone was distinguished from the transitional zone based on their anatomical boundaries. The central zone was not distinguished from the peripheral zone in this study due to difficult histologic differentiation and low incidence of prostate cancer in this zone.[34]

The prostate consists of three vertical regions: the apex, the middle region, and the base. The distal 5 mm of the prostate is the apex, the proximal 5–10 mm of the prostate constitutes the base, and the rest of the prostate is considered the middle region. Vertically, we divided the prostate into three approximately equal proportions (distal/middle/proximal) or into two parts (distal half/proximal half). The specific regional division of each layer is shown in Table S1. The location of each lesion was defined according to whether there was more than half of the cancerous area in the zone.

Statistical analysis

Statistical analyses were performed using SAS 9.4 software (SAS Institute Inc., Cary, NC, USA). The linear relationship between age and prevalence was assessed by the Cochran-Armitage test for trend.[35,36] We calculated the sensitivity and the relative 95% confidence interval (CI) for TP and TR biopsy in the diagnoses of prostate cancer and csPCa. Differences between the sensitivities of TP and TR biopsy were compared using McNemar's test.[37] We also conducted a subgroup analysis according to the ITV ($\leq$0.20 mL, [0.20, 0.50] mL, >0.50 mL) and GrG (1, $\geq$2, $\geq$3). For diagnosing neoplastic lesions, the subgroups were stratified by GrG and location. Cohen's kappa statistics were used for the TP and TR agreement analysis.[38]

Univariate and multivariate logistic regression analyses were conducted with the missed detection of tumor lesions as the outcome. Potential predictors included tumor volume (TV), PV, GrG, index status, and tumor location (anterior/posterior, peripheral zone [PZ]/transitional zone [TZ], and distal/proximal). Odds ratios (ORs) and 95% CIs were calculated. Predictors with $p < 0.1$ in univariate analysis were included in the multivariate model. A two-tailed p value < 0.05 was considered statistically significant for all analyses.

RESULTS

Epidemiological characteristics of latent prostate cancer

The median age of the decedents was 83 years (range 39–102 years, interquartile range: 73–89 years), and the median prostate volume was 40 mL (range 13–188 mL, interquartile range: 28–50 mL). The crude prevalence of latent prostate cancer was 35.1% (81/231, 95% CI: 29.1–41.8), with all 170 lesions pathologically confirmed as prostate carcinoma. Multifocality was observed in 52% of participants with latent prostate cancer. Sixty-five percent of participants with cancer had csPCa, with 10% having GrG 5 cancer (Table 1).

The prevalence of all prostate cancers and csPCa increased with age (all prostate cancers: p = 0.001; csPCa: p = 0.001) (Figure 3). Among people over 70 years old, 40% had latent prostate cancer, and 26% had csPCa (Figure 3). Among those older than 90 years, the prevalence of all prostate cancer and csPCa increased to 55% and 37%, respectively.

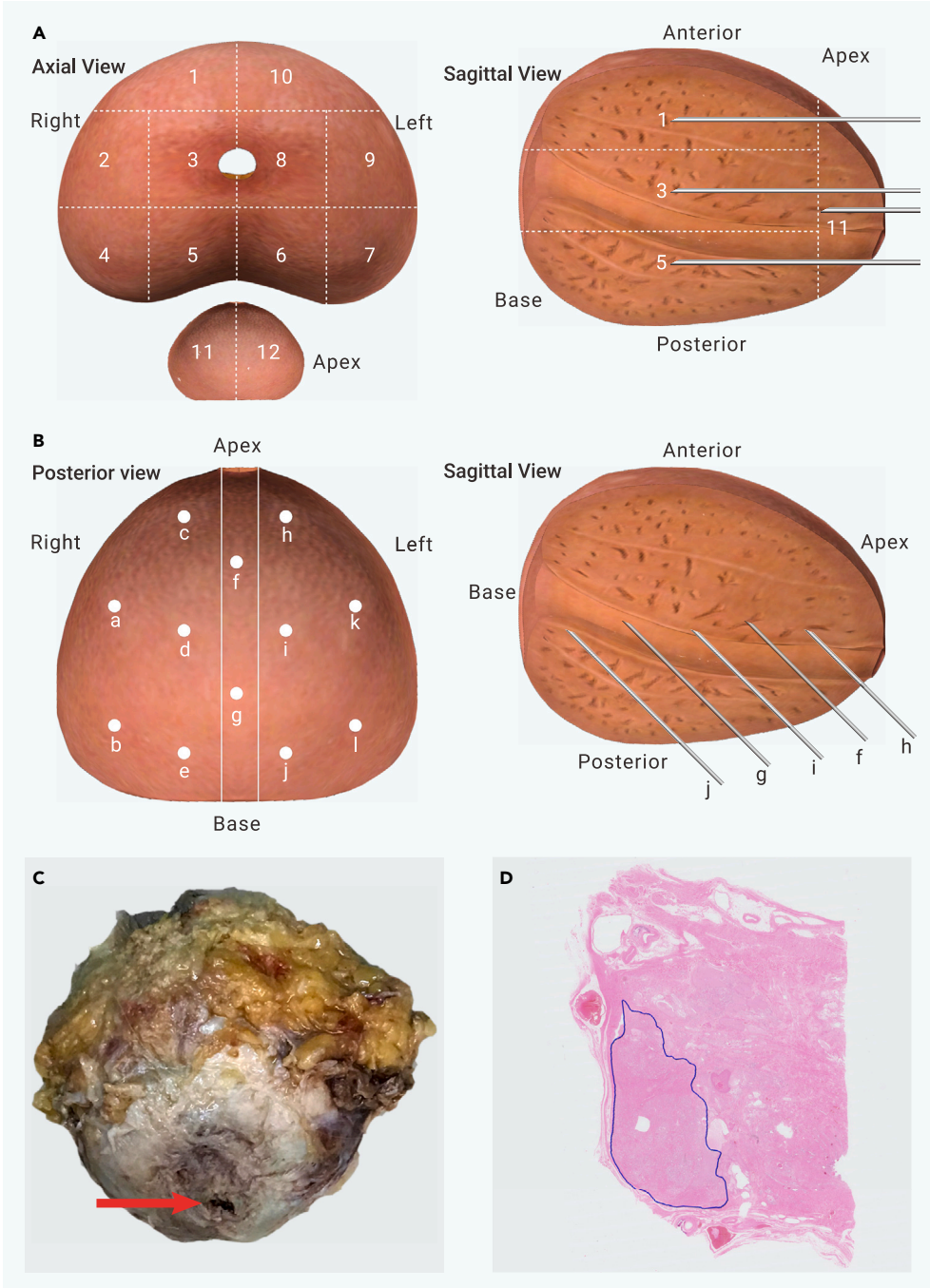


Figure 2. Biopsy plan, autopsy specimen, and digital slice (A) Five cores were obtained from each lobe for transperineal biopsy, with two cores targeting the apex. (B) Five cores were obtained from each lobe for transrectal biopsy, with two cores obtained near the midline. (C) Anterior view of a prostate after autopsy, with the distal end of the urethra marked with an arrow. (D) Digital slice and tumor lesion (outlined in blue).

Consistency between biopsy results and whole-mount pathology

The consistency rate to whole-mount pathology was not significantly different between TP and TR biopsy (78% vs. 73%, p = 0.501). The agreement between TP and TR biopsy was low for diagnosing cancer (kappa value 0.47, 95% CI: 0.26–0.67) (Table 2) and lesions (kappa value 0.42, 95% CI: 0.25–0.60) (Table 3), especially for cases with ITV $\leq$0.2 mL (kappa value 0.15, 95% CI: 0.26–0.67) and lesions $\leq$0.2 mL (kappa value 0.19, 95% CI: −0.04 to 0.42).

Characteristics of the detected and undetected lesions

Most undetected lesions had volumes $\leq$ 0.2 mL (93.6%) or GrGs = 1 (56.8%). Lesions detected by TP and TR had significantly higher volumes (TP: median 0.279 mL vs. 0.012 mL, p < 0.001; TR: median 0.240 mL vs. 0.013 mL, p < 0.001) and higher GrGs (p < 0.001) than undetected lesions. Lesions detected by TP and TR did not differ in volume (p = 0.227) or GrG (p = 0.811). Lesions in different locations exhibited similar rates of missed detection (Figure 4A).

In the univariate analysis, TV, GrG, and index status were significantly related to the missed detection of all lesions. Only TV remained an independent predictor in the multivariate analysis (OR 0.81 per 0.1 mL, 95% CI 0.67–0.98, p = 0.027) (Table S3).

All 17 lesions >0.5 mL were in the PZ and had a GrG $\geq$2. Both TP and TR methods of biopsy missed 35.3% (6/17) of these large lesions. Five large lesions were missed by both approaches, with the largest being 1.296 mL. Proportionally, more anterior large lesions (4/6) were missed than posterior lesions (1/11) (p = 0.028) (Figure 4B). None of them were in the proximal third of the prostate.

Diagnostic performance of TP and TR biopsy

There was no significant difference between the per-patient sensitivity of TP biopsy (33.3%, 95% CI: 23.1–43.6) and TR biopsy (32.1%, 95% CI: 21.9–42.3) in the overall population (p = 0.82) or in subgroup analyses according to ITV and GrG (Table 2). Among those with ITVs >0.5 mL, the sensitivity was 68.8% (11/16, 95% CI: 46.0–91.5) for TP biopsy and 75.0% (12/16, 95% CI: 53.8–96.2) for TR biopsy.

Vertically, TP biopsy had a higher per-lesion sensitivity than TR biopsy for csPCa lesions in the distal third (34.7% vs. 16.3%, p = 0.02) and distal half (30.6% vs. 18.1%, p = 0.04) of the prostate (Table 3). TR biopsy had a higher per-lesion sensitivity than TP biopsy in the proximal half of all lesions (25.0% vs. 13.9%, p = 0.046). There was no significant difference in the sensitivity of TP and TR biopsy for all tumors (p = 0.35) and csPCa lesions (p = 0.20).

The mean length of the biopsy cores was 11.7 ± 2.7 mm (range 5.6–18.0 mm) for TP biopsy and 11.8 ± 2.8 mm (range 4.9–18.0 mm) for TR biopsy. The total length of the tumor tissue was 454.1 mm for TP biopsy and 386.4 mm for TR biopsy. The characteristics of biopsy-positive and biopsy-negative cases are shown in Table S2.

DISCUSSION

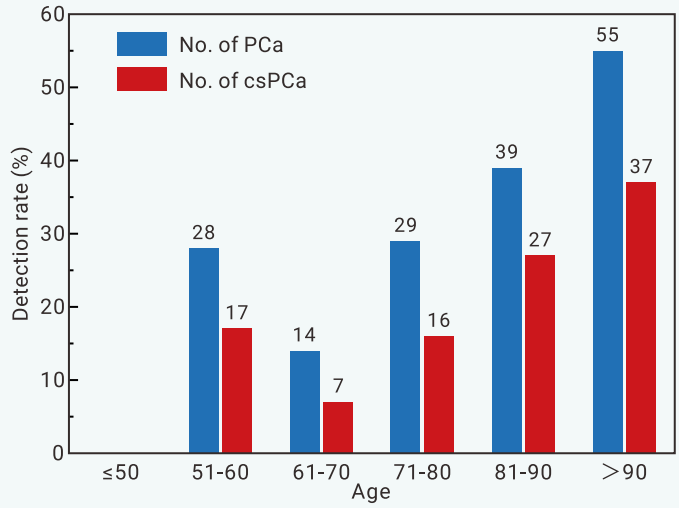
This study has been the largest autopsy study on latent prostate cancer in China in the past 2 decades. Due to the scarcity of body donors, the collection of autopsy specimens for this study lasted from 2014 to 2021.

In 1994, Gu et al. reported a crude prevalence of 4.7% for latent prostate cancer in Chinese males with a median age of 31–40 years and a prevalence of 25.0% in men older than 70 years.[5] In 2004, Zhang et al. reported a crude prevalence of 18.7% in men with an average age of 84 years.[6] In our preliminary study, latent prostate cancer was identified in 35.6% of cases undergoing autopsy.[7] With a larger sample size, we found that the crude prevalence was 35.1% among all men, 39.6% among men older than 70 years, and 55% among men older than 90. These statistics are similar to those reported for European decedents,[3] challenging the previous view that the prevalence of latent prostate cancer in China is markedly

Table 1. Demographic and clinical characteristics of body donors

Characteristics	With latent prostate cancer (n = 81)	Without latent prostate cancer (n = 150)
Age, y	86 (79–91)	80 (70–87)
≤70	9 (11.1)	40 (26.7)
71–80	15 (18.5)	36 (24.0)
81–90	36 (44.4)	57 (38.0)
>90	21 (25.9)	17 (11.3)
Cause of death		
Cardiovascular disease	24 (29.6)	35 (23.3)
Respiratory disease	28 (34.6)	44 (29.3)
Malignancies	17 (21.0)	49 (32.7)
Organ failure	11 (13.6)	10 (6.7)
Other	1 (1.2)	12 (8.0)
PV (mL)	40 (29–51)	37 (27–48)
Focality		
Unifocal	39 (48)	–
Multifocal	42 (52)	–
TTV (mL)	0.084 (0.015–0.386)	–
ITV (mL)	0.075 (0.013–0.299)	–
GrG		
1	28 (35)	–
2	33 (41)	–
3	8 (10)	–
4	2 (2)	–
5	10 (12)	–
Pathological T staging		
pT2	74 (91)	–
pT3a	3 (4)	–
pT3b	4 (5)	–

GrG, grade group; ITV, index tumor volume; PV, prostate volume; TTV, total tumor volume.



Age	≤50	51-60	61-70	71-80	81-90	>90
No. of decedents	2	18	29	51	93	38
No. of PCa	0	5	4	15	36	21
No. of csPCa	0	3	2	8	25	14

Figure 3. Prevalence of all prostate cancer and csPCa in different age groups The prevalence of all prostate cancers and csPCa increased with age.

lower than that in western populations. We speculated that large-scale screening through prostate-specific antigen (PSA) can substantially increase the diagnosis of clinical cancer, and raise the issues of overdiagnosis and overtreatment.

We also observed that csPCa and GrG 5 tumors constituted 65% and 10% of latent cancers, respectively. The proportion of csPCa ranged from 7% to 51% in other international studies.[25,28,39–45] Nevertheless, these high-grade latent cancers did not affect patients' survival. We hypothesized that a substantial proportion of patients undergoing radical clinical treatment are overtreated. Conversely, a recent 15-year follow-up study revealed that even a low-risk localized prostate cancer may finally metastasize and progress to a life-threatening tumor.[46] We proposed that the current pathological diagnostic criteria are inadequate for assessing the malignant behavior and prognosis of prostate cancer. Thus, future studies should explore alternative methods for precise diagnosis and treatment of prostate cancer.

The Cochran-Armitage test for trend showed an upward trajectory in the prevalence of all prostate cancer and csPCa with aging. However, we noticed that the prevalence in the 51–60 age group exceeded that in the 61–70 age group. This discrepancy may be due to two reasons. First, the limited sample size may have introduced some degree of fluctuation in the estimations. Second, the prevalence of prostate cancer may not increase in the Chinese population until the age of 70. A higher prevalence of prostate cancer in advanced ages has been similarly reported in other countries,[4] and aging is considered a major risk factor for prostate cancer.[47]

To our knowledge, this study is the first to compare the sensitivity of TP and TR biopsy rather than their detection rates. In our head-to-head comparison, systematic 12-core TP and TR biopsies exhibited comparable sensitivities for diagnosing prostate cancer in all cases and in ITV and GrG subgroups. Although the total tumor tissue obtained by TP biopsy was longer than that of TR, there was no significant difference in diagnosis consistency with whole-mount pathology.

Meanwhile, we observed different sensitivities of TP and TR biopsy methods for the distal and proximal parts of the prostate. We believe that the initial 12-core biopsy recommended by the current guideline[12] does not provide comprehensive coverage of the entire gland. Twelve-core TP biopsy has two cores specifically targeting the apical region; however, the biopsy depth is not sufficient to cover the proximal prostate. On the other hand, TR biopsy, in which the needles are inserted at a 45-degree angle to the posterior surface of the prostate, has poor coverage for the apical area due to angular restriction but is better for sampling the proximal prostate.

The majority of undetected lesions were smaller than 0.2 mL and had a GrG = 1 in this study. In multivariate analysis, TV was the only independent predictor of missed detection. GrG was not a significant predictor of missed detection, possibly because of its correlation with TV.[25] In our study, TP and TR biopsy exhibited low sensitivity and poor consistency for lesions of 0.2 mL or less, indicating inaccuracy of systematic biopsy in detecting small lesions.

According to the Epstein criteria,[48] tumors larger than 0.5 mL are considered clinically significant. Rocco et al. indicated that the sensitivity of 12-core TP prostate biopsy was 75% (9 of 12) for Epstein-significant cases.[27] Biopsy simulation by Haas et al. indicated that the sensitivity of 12-core TR biopsy for cases with ITV ≥0.5 mL is 85% (11 of 13).[25] In our study, the sensitivity of TP and TR methods of biopsy for cases with ITV ≥0.5 mL was 68.5% (11 of 16) and 75% (12 of 16), respectively. Our study supports previous findings by providing more autopsy cases. These data can help decision-making before and after a prostate biopsy.

Five out of 17 lesions larger than 0.5 mL were missed by both methods of biopsy, and four were in the anterior prostate, suggesting that the current biopsy

Table 2. Per-patient diagnostic performance of TP and TR biopsy

	Sensitivity, % (95% CI)			
	Transperineal	Transrectal	p	Kappa value, % (95% CI)
The patients with prostate cancer confirmed by pathology				
Overall (N = 81)	33.3 (23.1–43.6)	32.1 (21.9–42.3)	0.82	46.7 (26.3–67.2)
ITV ≤0.2 mL (n = 56)	17.9 (7.8–27.9)	17.9 (7.8–27.9)	1.00	14.8 (−15.2–44.7)
0.2 mL <ITV ≤0.5 mL (n = 9)	66.7 (35.9–97.5)	44.4 (12.0–76.9)	0.32	14.3 (−43.5–72.1)
ITV >0.5 mL (n = 16)	68.8 (46.0–91.5)	75.0 (53.8–96.2)	0.32	84.6 (55.8–100.0)
The patients with GrG ≥2 prostate cancer confirmed by pathology[a]				
Overall (N = 53)	45.3 (31.9–58.7)	35.9 (22.9–48.8)	0.23	34.1 (9.0–59.2)
ITV ≤0.2 mL (n = 28)	25.0 (9.0–41.0)	25.0 (9.0–41.0)	1.00	23.8 (−16.0–63.6)
0.2 mL <ITV ≤0.5 mL (n = 9)	66.7 (35.9–97.5)	22.2 (0.0–49.4)	0.10	−12.5 (−59.8–34.8)
ITV >0.5 mL (n = 16)	68.8 (46.0–91.5)	62.5 (38.8–86.2)	0.56	58.6 (17.2–100.0)
The patients with GrG ≥3 prostate cancer confirmed by pathology[a]				
Overall (N = 20)	55.0 (33.2–76.8)	40.0 (18.5–61.5)	0.18	51.0 (15.3–86.6)
ITV ≤0.2 mL (n = 6)	33.3 (0.0–71.1)	16.7 (0.0–46.5)	0.32	57.1 (−12.1–100.0)
0.2 mL <ITV ≤0.5 mL (n = 4)	50.0 (1.0–99.0)	–	–	–
ITV >0.5 mL (n = 10)	70.0 (41.6–98.4)	70.0 (41.6–98.4)	1.00	52.4 (−5.3–100.0)

ITV, index tumor volume.
[a]In the subgroup analysis of the patients with GrG ≥2 or GrG ≥3 prostate cancer, only a biopsy result with a GrG ≥2 was considered positive.

scheme may provide an insufficient sample of the anterior prostate. In TR biopsy, a needle is inserted through the rectum, which passes through the posterior wall of the prostate at an oblique angle. This approach can potentially decrease the detection rate in the anterior half of the prostate.[20,21] In TP biopsy, the needle is inserted parallel to the urethra, and the insertion points can be strategically chosen for effective sampling of the anterior portion of the prostate. The distribution of needle insertions in TP biopsy displayed a bias toward the posterior half of the prostate in our study. This might contribute to the missed diagnoses of lesions >0.5 mL in the anterior half in our TP biopsy cohort. For patients with a previously negative biopsy, we could mainly focus on the anterior prostate in suspicion cases. Whether the anterior prostate is an independent predictor of missed detection needs further verification with a larger sample size.

Magnetic resonance imaging (MRI)-targeted prostate biopsy has been proven effective and is commonly used in clinical practice.[49,50] Although systematic biopsy improved the detection of csPCa, it simultaneously increased overdiagnosis, which discourages its clinical application.[51] MRI has limited sensitivity for small lesions. Herein, in a large retrospective cohort study, MRI detected only 19% of the lesions with diameters of 6–10 mm.[52] Patients with undetected lesions are not included in the monitoring cohort, which can delay future diagnosis and affect patients' survival. Therefore, the overdiagnosis associated with systematic biopsy is acceptable with the current diagnostic tools, as treatment can be more conservative.

Our study has several limitations. First, the study population mainly consisted of middle-aged and elderly body donors with no PSA data or imaging findings. Second, due to technical difficulties, ultrasonography- or MRI-targeted biopsy was not performed in our autopsy study. Third, the limited sample size of the autopsy prostates might have undermined some differences.

CONCLUSION

Compared with previous studies, the prevalence of latent prostate cancer has increased in China. No significant differences were detected between the sensitivities of systematic 12-core TP and TR biopsies when considering whole-mount pathology as the gold standard. TP biopsy was superior in diagnosing csPCa lesions in the distal portion of the prostate, while TR biopsy detected more lesions in the proximal portion. Approximately one-third of lesions larger than 0.5 mL were missed by TP or TR biopsy, and most of these lesions were located in the anterior prostate.

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Table 3. Per-lesion diagnostic performance of transperineal and transrectal biopsy

	Sensitivity, % (95% CI)			
	Transperineal	**Transrectal**	**p**	**Kappa value, % (95% CI)**
All lesions confirmed by pathology				
Overall (N = 170)	19.4 (13.5–25.4)	16.5 (10.9–22.1)	0.35	42.2 (24.7–59.6)
Anterior (n = 90)	18.9 (10.8–27.0)	14.4 (7.2–21.7)	0.35	28.3 (3.4–53.1)
Posterior (n = 80)	20.0 (11.2–28.8)	18.8 (10.2–27.3)	0.76	56.0 (32.9–79.1)
Peripheral zone (n = 151)	20.5 (14.1–27.0)	16.6 (10.6–22.5)	0.26	38.8 (20.4–57.2)
Transitional zone (n = 19)	10.5 (0.0–24.3)	15.8 (0.0–32.2)	0.32	77.1 (34.6–100.0)
Distal (n = 84)	23.8 (14.7–32.9)	15.5 (7.7–23.2)	0.09	36.6 (12.8–60.4)
Middle (n = 76)	15.8 (7.6–24.0)	17.1 (8.6–25.6)	0.76	47.4 (20.8–73.9)
Proximal (n = 10)	10.0 (0.0–28.6)	20.0 (0.0–44.8)	0.32	61.5 (−4.5–100.0)
Distal half (n = 134)	20.9 (14.0–27.8)	14.2 (8.3–20.1)	0.07	36.0 (16.2–55.8)
Proximal half (n = 36)	13.9 (2.6–25.2)	25.0 (10.9–39.1)	**0.046**	65.2 (35.1–95.4)
Lesions with GrG ≥2 confirmed by pathology[a]				
Overall (N = 91)	29.7 (20.3–39.1)	23.1 (14.4–31.7)	0.20	38.1 (17.1–59.1)
Anterior (n = 49)	26.5 (14.2–38.9)	18.4 (7.5–29.2)	0.29	18.7 (−11.3–48.7)
Posterior (n = 42)	33.3 (19.1–47.6)	28.6 (14.9–42.2)	0.48	55.6 (28.5–82.6)
Peripheral zone (n = 86)	29.1 (19.5–38.7)	23.3 (14.3–32.2)	0.28	37.1 (15.3–58.9)
Transitional zone (n = 5)	40.0 (0.0–82.9)	20.0 (0.0–55.1)	0.32	54.6 (−16.4–100.0)
Distal (n = 49)	34.7 (21.4–48.0)	16.3 (6.0–26.7)	**0.02**	22.9 (−3.8–49.5)
Middle (n = 39)	23.1 (9.9–36.3)	30.8 (16.3–45.3)	0.26	54.7 (25.6–83.9)
Proximal (n = 3)	33.3 (0.0–86.7)	33.3 (0.0–86.7)	1.00	100.0 (100.0–100.0)
Distal half (n = 72)	30.6 (19.9–41.2)	18.1 (9.2–26.9)	**0.04**	29.8 (6.2–53.4)
Proximal half (n = 19)	26.3 (6.5–46.1)	42.1 (19.9–64.3)	0.08	65.9 (32.6–99.2)

[a]In the subgroup analysis of the lesions with GrG ≥2, only a biopsy result with GrG ≥2 was considered positive.

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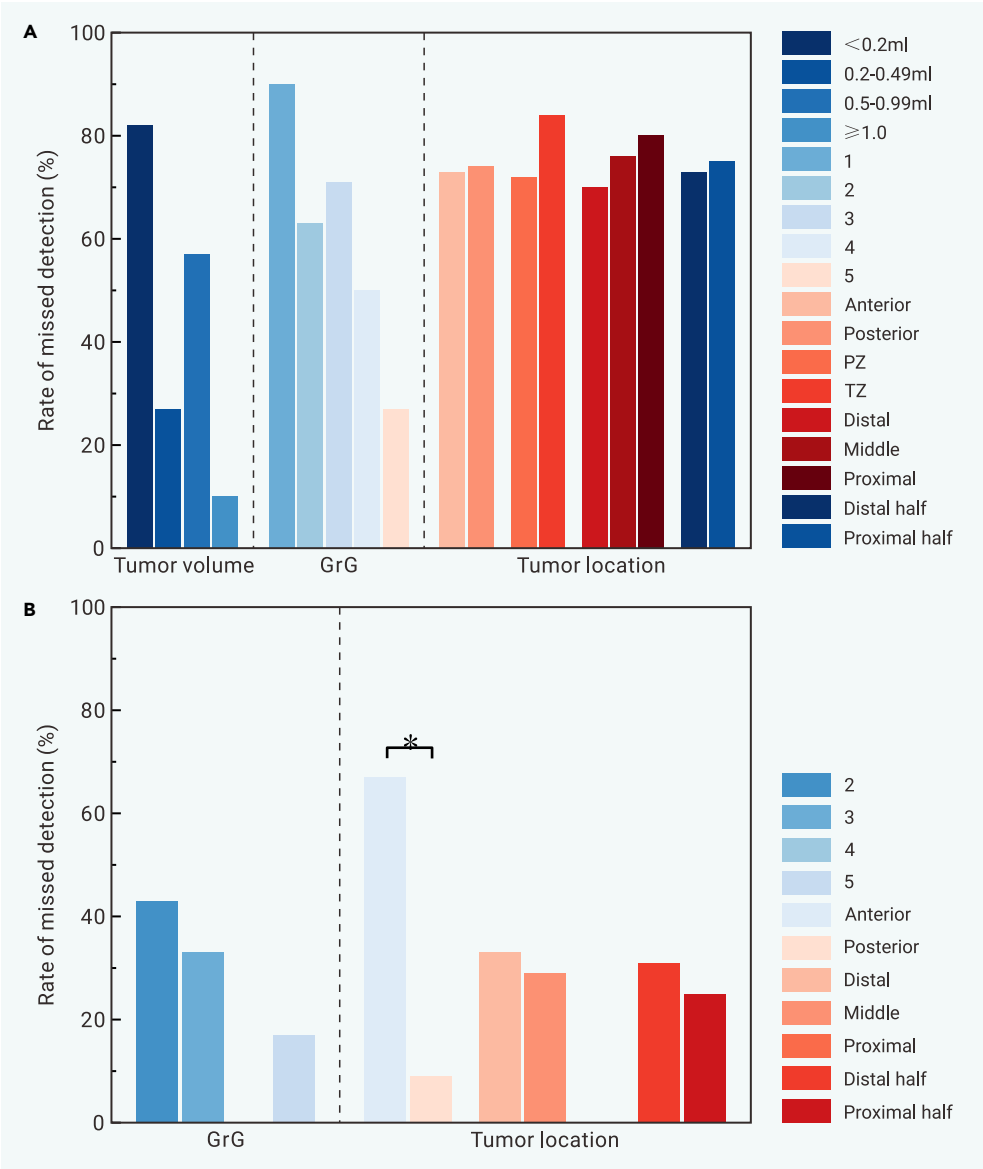

Figure 4. Rates of lesions missed by both TP and TR methods of biopsy, stratified by tumor volume (TV), grade group (GrG), and tumor location (A) Among all lesions (n = 170), the rate of missed detection showed a negative correlation with TV and GrG, and lesions in different locations had similar rates of missed detection. (B) All lesions >0.5 mL (n = 17) were in the peripheral zone and had GrG ≥2. *p < 0.05.

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Conceptualization, W.Y.; Project administration, W.Y.; Data curation, Y.C., Y.Zhou, Z.M., and Z.S.; Investigation, Y.C., Z.Z., Y.Zhou, Z.M., Z.S., Y.Zuo, Y.X., and W.W.; Formal analysis, Y.C., Y.Zhou, and H.W.; Writing – original draft, Y.C., Z.Z., Y.Zhou, and Y.Zuo; Methodology, Z.Z. Z.M., Y.X., H.W., and W.Y.; Writing – review & editing, Z.M., S.J., Z.L., Z.S., Y.X., W.W., H.W., and W.Y.; Literature search, S.J., Z.L., and Y.Zuo.

DECLARATION OF INTERESTS

The authors declare no competing interests.

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