Superior cancer detection with transperineal biopsy in patients with an elevated prostate-specific antigen level and a PI-RADS score of 3-4: A retrospective cohort study

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Abstract. The early and accurate detection of prostate cancer remains pivotal for improving clinical outcomes. The present study aimed to compare the cancer detection rates (CDRs) and safety profiles of transperineal (TP) vs. transrectal (TR) prostate biopsy techniques in patients with elevated prostate-specific antigen (PSA) levels and magnetic resonance imaging findings suggestive of malignancy (Prostate Imaging Reporting and Data System score 3 or 4). A retrospective cohort study was conducted on 127 patients who underwent TP (n=65) or TR (n=62) prostate biopsies between May 2022 and August 2024. CDR, adverse events and laboratory findings were compared between the groups. The TP approach yielded a significantly higher CDR (55.38%) than the TR approach (27.42%) (P=0.001), with no increase in adverse events, such as fever, infection or rectal bleeding. Routine lab values, including those for PSA and free PSA, showed no significant differences. In conclusion, in the present retrospective single-center cohort, the TP protocol used was associated with a higher cancer detection rate than the TR protocol, without an increased rate of adverse events. Given the non-randomized design and protocol differences between groups, these findings should be interpreted with caution and warrant confirmation in prospective multicenter studies.

Introduction

Prostate cancer (PCa) remains one of the most prevalent malignancies among men worldwide, ranking as the second most commonly diagnosed cancer and the fifth leading cause of cancer-related mortality in men globally (1,2). Early detection and an accurate diagnosis are pivotal in improving the prognosis and tailoring effective treatment strategies (3). Prostate-specific antigen (PSA) levels and magnetic resonance imaging (MRI) have emerged as essential tools for the identification and management of PCa (4,5). Elevated PSA levels often trigger further investigation through prostate biopsies, while MRI provides detailed visual assessments, utilizing the Prostate Imaging Reporting and Data System (PI-RADS), a standardized MRI reporting and risk stratification system for prostate lesions, to categorize abnormalities, with scores reflecting the likelihood of clinically significant PCa (6,7). Particularly, patients exhibiting a PI-RADS score of 3 or 4 represent a group requiring careful diagnostic exploration given their moderate to high suspicion of malignancy (8).

Traditionally, prostate biopsies have been performed via the transrectal (TR) approach, largely due to the accessibility of the prostate via the rectal wall (9). This method, although widely adopted, is not without its challenges, particularly the risk of infection due to the proximity to the rectal flora and the technical difficulty in sampling areas such as the anterior fibromuscular stroma and the transition zone of the prostate (10,11). The transperineal (TP) approach has gained attention as an alternative technique, aiming to address some of these limitations (12). By accessing the prostate through the perineum, this method potentially provides a more comprehensive sampling of the gland, especially the anterior and apical regions that are frequently undersampled in TR biopsies (13).

The anatomical advantages of the TP route may offer an enhanced cancer detection rate (CDR), which is an important consideration in clinical decision-making (14). Despite these potential advantages, the adoption of the TP technique in clinical practice has been hampered by perceived complexities and the need for specialized equipment and expertise (15). However, with advancements in technology and procedural techniques, the use of the TP approach as a standard practice has become increasingly more feasible (16). Nevertheless, comprehensive comparative studies examining the effectiveness of TP vs. TR biopsy techniques in real-world clinical settings remain limited (17).

Therefore, the present study aimed to compare the diagnostic yield and safety of TP vs. TR biopsy approaches in patients with elevated PSA levels and lesions with a PI-RADS

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score of 3 or 4. Given the clinical uncertainty in managing this intermediate-risk group, the findings are expected to provide practical evidence to guide biopsy strategy and optimize PCa detection.

Materials and methods

Case selection. The present retrospective cohort study included 127 male patients with elevated PSA levels and suspicions of PCa without a prior pathological diagnosis, identified by PI-RADS scores of 3 or 4, who were admitted to Anqing Municipal Hospital (Anqing, China) between May 2022 and August 2024. The mean age of the cohort was 69.79±7.45 years, with an age range of 55-80 years. These patients were divided into two groups based on the biopsy method used: The TP group (n=65) and the TR group (n=62). Sample size was based on available patient data during the study period; no a priori power calculation was performed due to the retrospective nature of the study. Demographic information, general data, complete blood counts, urinalysis results and adverse reactions were collected from the patients' medical records.

This study was conducted in compliance with the Declaration of Helsinki, and approved by the Institutional Review Board and Medical Ethics Committee of Anqing Municipal Hospital [approval no. Medical Ethics Review (2025) no. 54]. The requirement for informed consent was waived due to the retrospective nature of the study, as it involved only de-identified patient data and posed no risk or impact on patient care. The waiver was granted in compliance with regulatory and ethical guidelines relevant to retrospective research studies.

Patients were assigned to the TP or TR group based on the institutional clinical practice protocol implemented during the study period. Specifically, the TR approach was the standard procedure before January 2023. From January 2023 onwards, the TP approach was gradually promoted as a preferred protocol, in conjunction with advancements in ultrasound elastography equipment (Mindray Resona R9S with ELC 13-4U probe; Shenzhen Mindray Bio-Medical Electronics Co., Ltd.) and the accumulation of operator experience in TP biopsy. Additionally, patient preference for anesthesia (TP with local anesthesia vs. TR without anesthesia) and equipment availability were taken into account during group assignment. Notably, the TP protocol differed from the TR protocol not only in terms of the biopsy route but also with regard to the sampling core number (12-13 cores for TP vs. 10-12 cores for TR), imaging guidance [elastography + two-dimensional (2D) ultrasound for TP vs. standard 2D transrectal ultrasound for TR] and cognitive MRI-targeted biopsy strategies, which should be considered when interpreting the results.

Inclusion and exclusion criteria. Inclusion criteria for the study were as follows: i) Patients with persistently elevated PSA levels, defined as total PSA (tPSA) >4 ng/ml, which was selected based on the conventional clinical threshold commonly used to prompt further evaluation for possible PCa (4,18), and a documented increase in PSA over time based on at least two measurements obtained ≥6 months apart. PSA velocity was retrospectively estimated as the annualized change between the earliest and most recent PSA values, without applying a predefined velocity cutoff; ii) patients with a PI-RADS score of 3 or 4; iii) patients aged ≥55 years; iv) patients without clinically significant coexisting conditions; and v) all enrolled patients fulfilled both the PSA-based inclusion criteria and MRI findings (PI-RADS 3-4); no patients were included solely based on MRI findings.

Exclusion criteria included: i) Patients who had previously undergone hormonal, surgical or radiation therapies for prostate diseases, or those with a history of repeated biopsies; ii) patients with inadequate samples for PCa analysis; iii) patients >80 years; iv) patients with uremia, uncontrolled hypertension or bleeding disorders; v) patients on anticoagulant or antiplatelet medications, to reduce the risk of bleeding complications associated with biopsy procedures; and vi) patients exhibiting symptoms of urinary tract infection or acute urinary retention.

Examination method. All procedures were performed by urologists with ≥5 years of experience in prostate biopsies to minimize operator-related variability.

TP biopsy was performed in the lithotomy position. The perineum was thoroughly disinfected. A total of 10 ml of 2% lidocaine was injected into the perineal and periprostatic tissues using a 21G subcutaneous injection needle for local anesthesia. Subsequently, under the guidance of an ultrasound dual-plane probe, a 18G automatic biopsy gun was used to collect tissue samples from 12-13 locations through the perineum, including the left anterior outer, left middle outer, left posterior outer, left anterior inner, left middle inner, left posterior inner, right anterior outer, right middle outer, right posterior outer, right anterior inner, right middle inner and right posterior inner, as well as the target area. The slightly higher number of samples in the TP group reflected its superior access to anterior and apical zones, enabling consistent adherence to a full extended-template scheme. On average, 2.1±0.6 MRI-targeted cores were obtained in the TP group. The ultrasound device used was the Mindray Resona R9S, manufactured by Shenzhen Mindray Bio-Medical Electronics Co., Ltd., equipped with an ELC 13-4U probe. The ultrasound elastography provides detailed visualization of the prostate's stiffness, which can help identify suspicious areas for targeted biopsies (Fig. 1A). Additionally, conventional 2D ultrasound imaging offers clear anatomical landmarks for guiding the biopsy needle accurately (Fig. 1B and C).

TR prostate biopsy was performed with the patients in the lateral decubitus position. The rectal area was prepared using a standard cleansing method. No local anesthesia or analgesics were administered prior to the procedure. Under the guidance of TR ultrasound, a spring-loaded 18G automatic biopsy gun was used to collect tissue samples from 10-12 locations through the rectum, including the left anterior outer, left middle outer, left posterior outer, left anterior inner, left middle inner, left posterior inner, right anterior outer, right middle outer, right posterior outer, right anterior inner, right middle inner and right posterior inner, as well as the target area. The puncture sites for TR biopsy were not fixed but were determined based on the operator's judgment and the patient's anatomical structures. Due to limitations in anterior zone access via the rectal route, the TR group occasionally received slightly fewer cores, and targeted biopsy was more dependent

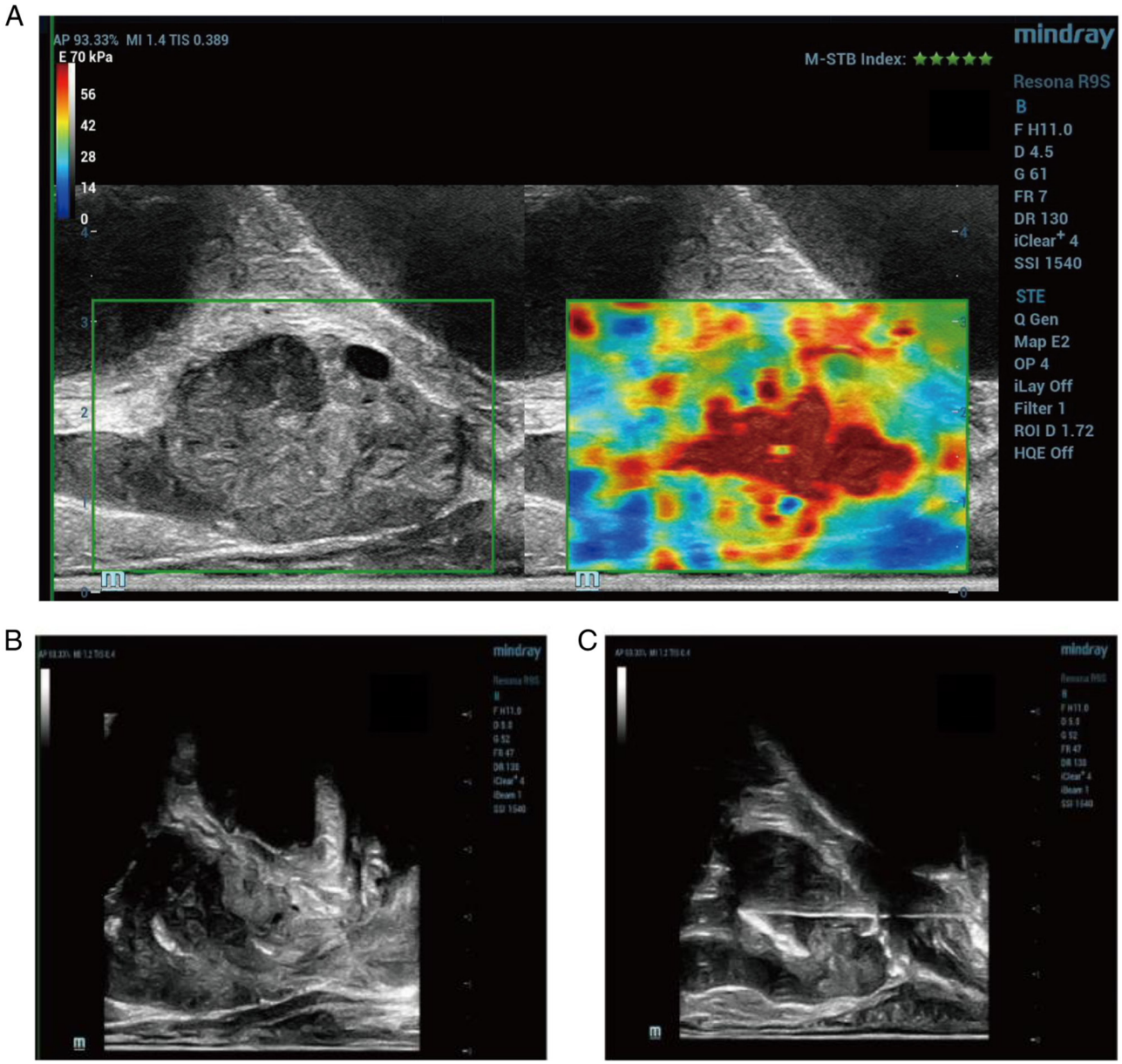

Figure 1. TP biopsy imaging. (A) TP ultrasound elastography image. (B) TP ultrasound two-dimensional image. (C) TP prostate biopsy image. TP, transperineal prostate.

on operator interpretation. The mean number of MRI-targeted cores in the TR group was 2.0±0.5.

Following the biopsy, patients were prescribed a 5-day course of oral ciprofloxacin at 500 mg twice daily and oral metronidazole at 400 mg three times daily. Patients returned for follow-up visits on the 7th and 30th days post-procedure, during which a questionnaire assessed surgical-related complications. Any rectal bleeding occurring immediately or within 1 month of the procedure was classified as post-procedural rectal bleeding or as rectal bleeding during the procedure causing hemodynamic changes. All patients, regardless of biopsy approach, received the same postoperative antibiotic regimen, consisting of oral ciprofloxacin at 500 mg twice daily plus oral metronidazole at 400 mg three times daily for 5 days. Although TP biopsy is associated with a lower risk of infectious complications, a uniform protocol was applied to both TP and TR groups in accordance with the institutional standard during the study period to ensure safety and procedural consistency.

Adverse event assessment. Adverse events were defined and graded according to the Clavien-Dindo classification system: Grade 1 (mild, no need for treatment), grade 2 (moderate, requiring medical treatment), grade 3 (severe, requiring invasive intervention), grade 4 (life-threatening) and grade 5 (death) (19). Specific complications included fever (body temperature >38.0˚C), infection (clinical symptoms of urinary tract infection or sepsis confirmed by laboratory tests), hematuria (macroscopic hematuria lasting >24 h), urinary retention (inability to urinate requiring catheterization) and rectal bleeding (macroscopic rectal bleeding). All patients were followed up at 7 days and 30 days post-biopsy to assess the occurrence of adverse events, and relevant data were recorded in detail.

Routine examination. Before undergoing a biopsy, patient demographic characteristics and laboratory test results were collected, including complete blood counts, coagulation profiles, urinalysis, and serum levels of total PSA (tPSA) and free PSA (fPSA). All patients received comprehensive prostate evaluations comprising digital rectal examinations (DREs), prostate volume measurements and multiparametric MRI.

MRI scans were reviewed independently by two radiologists with >5 years of experience in genitourinary imaging, and lesions were scored according to PI-RADS v2.1 criteria (7). Discrepancies in interpretation were resolved through joint consensus. MRI-targeted biopsies were performed using a cognitive fusion approach, in which pre-identified MRI lesions were mentally co-registered with real-time ultrasound images during the procedure. In the TP group, biopsies were guided using the Mindray Resona R9S system equipped with both high-resolution B-mode imaging and real-time elastography, enhancing visualization and targeting of suspicious areas. By contrast, the TR group utilized standard 2D TR ultrasound probes without elastography or software-based fusion support. This difference in imaging capabilities may have contributed to variations in lesion detection between the two groups.

Puncture biopsy results. The primary endpoint of this study was the CDR. In accordance with the World Health Organization Tumor Classification of the Prostate (20), biopsy cores showing acinar adenocarcinoma, neuroendocrine tumors, mesenchymal tumors or other malignant findings were classified as positive. Conversely, pathological diagnoses such as benign prostatic hyperplasia, prostatitis, prostatic intraepithelial neoplasia, atypical small acinar proliferation or other non-malignant findings were considered negative. Clinically significant PCa (csPCa) was defined as International Society of Urological Pathology (ISUP) Grade Group ≥2 (corresponding to Gleason score ≥7), based on the ISUP grading system described in the 2022 World Health Organization Classification of Tumors of the Urinary System and Male Genital Organs (20). csPCa detection rate (csCDR) was defined as the proportion of patients diagnosed with csPCa among all patients in each group and was used as a secondary endpoint to evaluate the diagnostic performance of the biopsy techniques. The rate of positive biopsy cores was calculated as the number of cancer-positive cores divided by the total number of biopsy cores obtained for each patient and was used as an indicator of cancer detection per core.

Statistical analysis. The data were analyzed using SPSS statistical software, version 29.0 (IBM Corp.). Continuous variables were initially assessed for normal distribution using the Shapiro-Wilk test. Normally distributed continuous data are presented as the mean ± standard deviation and were compared between groups using the independent-samples t-test. Non-normally distributed data are expressed as the median (25th percentile-75th percentile) and were analyzed using the Wilcoxon rank-sum test. Categorical variables are presented as n (%) and were compared using the χ^2 test or Fisher's exact test, as appropriate. Fisher's exact test was used when the assumptions for the $\chi 2$ test were not met, including when expected cell counts were small. Two-sided $P<0.05$ was considered to indicate a statistically significant difference.

In addition, univariate logistic regression was performed to screen potential variables, and variables with $P<0.2$ were considered candidate variables for inclusion in the multivariate analysis. A multivariate logistic regression model was then constructed using a bidirectional stepwise selection approach to identify independent factors associated with PCa detection.

Results

Baseline characteristics. The baseline demographics and clinical features of the TP and TR groups are summarized in Table I. No statistically significant differences were observed for age, BMI, smoking and alcohol history, or the prevalence of hypertension between the TP and TR groups ($P>0.05$). However, the TP group had a significantly higher prevalence of diabetes (12.31 vs. 1.61%; $P=0.045$).

The CDR was significantly higher in the TP group (55.38%) compared with that in the TR group (27.42%) ($P=0.001$), indicating a diagnostic advantage of the TP technique.

Laboratory parameters, including complete blood count and cancer markers, were comparable between groups, except for a lower urinary pH observed in the TP group ($P=0.033$).

Adverse symptoms. Both groups reported no instances of urinary incontinence. The incidence of hematuria was low and identical in both groups, occurring in 2 patients (3.08% in the TP group and 3.23% in the TR group; $\chi^2=0.000$; $P=1.000$). Dysuria was reported by 58.46% of patients in the TP group and 66.13% in the TR group ($\chi^2=0.794$; $P=0.373$). Difficulty in bowel movements was reported in 2 patients (3.08%) in the TP group and in no patients (0.00%) in the TR group ($P=0.497$). These results indicate that adverse symptoms were comparable between the two biopsy techniques, with no significant differences observed (Table II).

Cancer markers. PSA levels were similar between the groups, with median values and interquartile ranges of 11.95 (7.65-18.1) ng/ml for the TP group and 12.46 (7.09-22.84) ng/ml for the TR group ($W=2021.000$; $P=0.979$) (Fig. 2). Similarly, fPSA levels and the fPSA/tPSA (f/t PSA) ratio did not differ significantly, with the TP group showing median fPSA levels of 1.84 (1.12-2.89) ng/ml compared with 1.99 (1.33-3) ng/ml in the TR group ($W=1790.000$; $P=0.279$), and f/t PSA ratios of 0.15 (0.11-0.23) compared with 0.16 (0.11-0.26) ($W=1879.000$; $P=0.513$). These findings demonstrate that the cancer marker profiles were comparable between patients undergoing TP and TR biopsy techniques, with no significant disparities observed.

Prostate examination results. DRE outcomes showed a high prevalence of abnormalities in both groups, with 96.92% in the TP group and 98.39% in the TR group ($\chi^2=0.962$; $P=0.618$) (Table III). These results indicate that the vast majority of patients in both groups had palpable abnormalities on DRE. MRI results based on PI-RADS scores were also similar between groups. For the TP group, 56.92% of patients had PI-RADS 3 lesions and 43.08% had PI-RADS 4 lesions, while in the TR group, 56.45% had PI-RADS 3 and 43.55% had PI-RADS 4 lesions ($\chi^2=0.003$; $P=0.957$). The distribution of ISUP Grade Groups (Gleason score) among patients diagnosed with PCa is also shown in Table III.

Table I. Baseline characteristics of participants in the TP (n=65) and TR (n=62) groups.

Parameters	TP	TR	Test statistic	P-value
Mean age ± SD, years	69.37±6.88	70.23±8.00	0.648[a]	0.518
Mean BMI ± SD, kg/m^2	22.94±2.63	22.70±3.33	0.454[a]	0.650
Smoking history, n (%)			2.843[b]	0.092
No	47 (72.31)	36 (58.06)		
Yes	18 (27.69)	26 (41.94)		
Alcohol consumption history, n (%)			0.130[b]	0.718
No	56 (86.15)	52 (83.87)		
Yes	9 (13.85)	10 (16.13)		
Hypertension, n (%)			0.003[b]	0.957
No	37 (56.92)	35 (56.45)		
Yes	28 (43.08)	27 (43.55)		
Diabetes, n (%)			4.008[c]	0.045[d]
No	57 (87.69)	61 (98.39)		
Yes	8 (12.31)	1 (1.61)		
Cancer detection rate, n (%)			10.206[b]	0.001[d]
Not detected	29 (44.62)	45 (72.58)		
Detected	36 (55.38)	17 (27.42)		
Mean red blood cell count ± SD (x10^{12}/l)	4.39±0.42	4.27±0.50	1.432[a]	0.155
Mean hemoglobin ± SD, g/l	134.98±14.82	130.52±13.38	1.781[a]	0.077
White blood cell count (x10^9/l)[f]	5.83 (4.77-7.68)	5.66 (4.86-7.36)	0.229[e]	0.819
Platelet count (x10^9/l)[f]	183 (156-214)	180 (146.25-228.75)	0.363[e]	0.716
pH level[f]	5.5 (5-6)	6 (5.5-6.5)	2.130[e]	0.033[d]
Specific gravity[f]	1.02 (1.02-1.02)	1.02 (1.01-1.02)	1.852[e]	0.064

[a]Independent-samples t-test; [b]χ^2 test; [c]Fisher's exact test; [d]P<0.05; [e]Wilcoxon rank-sum test. [f]Data are presented as the median (25th percentile-75th percentile). BMI, body mass index; TP, transperineal; TR, transrectal.

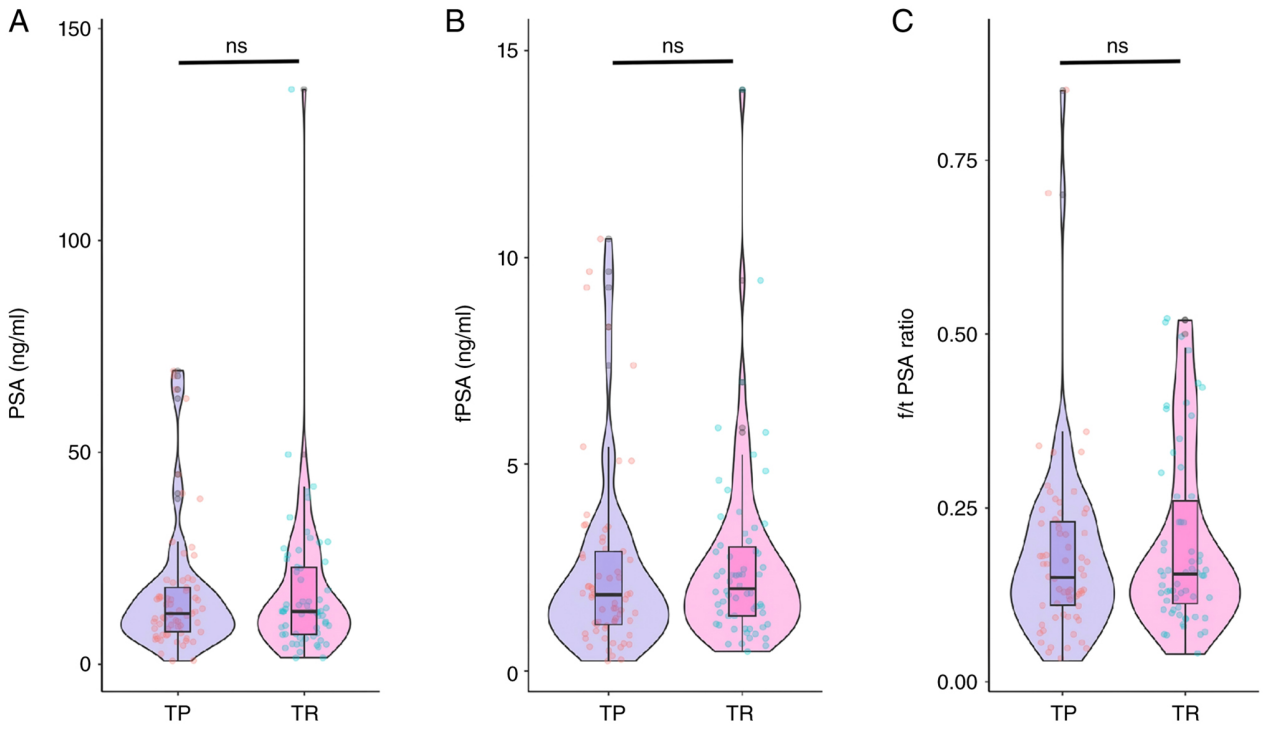

Figure 2. Comparison of PSA and fPSA levels between two groups of patients. (A) PSA; (B) fPSA; and (C) f/t PSA. f/t, free/total; PSA, prostate-specific antigen; ns, not significant.

Table II. Comparison of adverse symptoms of patients in the TP (n=65) and TR (n=62) groups.

Parameters	TP	TR	Test statistic	P-value
Urinary incontinence, n (%)			-	1.000
Absent	65 (100.00)	62 (100.00)		
Present	0 (0.00)	0 (0.00)		
Hematuria, n (%)			0.000	1.000
Absent	63 (96.92)	60 (96.77)		
Present	2 (3.08)	2 (3.23)		
Difficulty in bowel movements, n (%)			0.461	0.497
Absent	63 (96.92)	62 (100.00)		
Present	2 (3.08)	0 (0.00)		

Categorical variables were compared using the χ^2 test or Fisher's exact test, as appropriate. Fisher's exact test was used when expected cell counts were small. TP, transperineal; TR, transrectal.

Table III. Comparison of prostate examination results between the TP (n=65) and TR (n=62) groups.

Parameters	TP	TR	Test statistic	P-value
Digital rectal examination, n (%)			0.962	>0.999
Normal	2 (3.08)	1 (1.61)		
Abnormal	63 (96.92)	61 (98.39)		
MRI results, n (%)			0.003	0.957
PI-RADS score=3	28 (43.08)	27 (43.55)		
PI-RADS score=4	37 (56.92)	35 (56.45)		
Prostate volume, n (%)			-	0.488
Normal (≤30 ml)	0 (0.00)	1 (1.61)		
Abnormal (>30 ml)	65 (100.00)	61 (98.39)		
Gleason grade			3.260	0.196
1	11 (16.92)	5 (8.06)		
2	32 (49.23)	9 (14.52)		
3	13 (20.00)	9 (14.52)		

Prostate volume was categorized as 'normal' if ≤30 ml and 'abnormal' if >30 ml, based on commonly accepted clinical thresholds for prostate enlargement. Categorical variables were compared using the χ^2 test or Fisher's exact test, as appropriate. Fisher's exact test was used when expected cell counts were small. MRI, magnetic resonance imaging; PI-RADS, Prostate Imaging Reporting and Data System; TP, transperineal; TR, transrectal.

Among all enrolled patients, 56 patients (86.15%) in the TP group and 23 patients (37.10%) in the TR group were diagnosed with PCa (ISUP Grade Group ≥1). Specifically, the TP group included 11 patients (16.92%) with Gleason Grade 1, 32 patients (49.23%) with Grade 2 and 13 patients (20.00%) with Grade 3. The TR group included 5 patients (8.06%) with Grade 1, 9 patients (14.52%) with Grade 2 and 9 patients (14.52%) with Grade 3. No patients in either group were classified as Grade 4 or 5. These findings indicate that the distribution of MRI-detected abnormalities, as reflected by PI-RADS categories, was comparable between the two biopsy techniques. Prostate volume assessments indicated nearly all patients in both groups had abnormal volumes (P=0.488), with only 1 patient in the TR group presenting with a normal volume. This suggests that nearly all patients in both groups had enlarged prostates, which is consistent with the clinical suspicion of PCa or benign prostatic hyperplasia.

Puncture biopsy results and adverse reactions. The analysis revealed a significantly higher rate of positive biopsy cores in the TP group, with a median of 8.30% (IQR, 0.00-33.3%) compared with 0.0% (IQR, 0.00-9.57%) in the TR group (W=2569.000; P=0.003) (Table IV). This rate, defined as the proportion of cancer-positive cores among the total number of biopsy cores obtained, was used as an indicator of cancer detection per core. Notably, this per-core detection rate remained significantly higher in the TP group, indicating that the superior cancer detection associated with TP biopsy persisted even after accounting for differences in the total number of biopsy cores obtained between the two groups.

Table IV. Comparison of puncture biopsy results and biopsy-related adverse reactions between the TP (n=65) and TR (n=62) groups.

Parameters	TP	TR	Test statistic	P-value
Median positive biopsy core rate (IQR), %	8.30 (0.00-33.30)	0 (0.00-9.57)	2,569.000	0.003
Fever, n (%)			-	1.000
Absent	65 (100.00)	62 (100.00)		
Present	0 (0.00)	0 (0.00)		
Infection, n (%)			-	1.000
Absent	65 (100.00)	62 (100.00)		
Present	0 (0.00)	0 (0.00)		
Rectal bleeding, n (%)			-	0.488
Absent	65 (100.00)	61 (98.39)		
Present	0 (0.00)	1 (1.61)		
Urinary retention requiring catheterization or medical intervention, n (%)				1.000
Absent	65 (100.00)	62 (100.00)		
Present	0 (0.00)	0 (0.00)		
Transient difficulty in urination [n (%)]			0.794	0.373
Absent	27 (41.54)	21 (33.87)		
Present	38 (58.46)	41 (66.13)		

The positive biopsy core rate was compared using the Wilcoxon rank-sum test. Categorical variables were compared using the χ^2 test or Fisher's exact test, as appropriate. Urinary retention requiring catheterization or medical intervention was defined as Clavien-Dindo Grade ≥2. Transient difficulty in urination was classified as Clavien-Dindo Grade 1 as it resolved spontaneously without catheterization or additional intervention. TP, transperineal; TR, transrectal. IQR, interquartile range.

Adverse reactions were infrequent in both groups and showed no statistically significant differences. No cases of fever or infection were observed. Rectal bleeding occurred in only one patient in the TR group (1.61%; P=0.488) (Table IV). No urinary retention requiring catheterization or medical intervention (Clavien-Dindo Grade ≥2) was observed in either group. Transient difficulty in urination (Clavien-Dindo Grade 1) was reported in 38 patients (58.46%) in the TP group and 41 patients (66.13%) in the TR group, with no significant difference between groups (χ^2=0.794; P=0.373). These events resolved spontaneously without catheterization or additional intervention and are presented in Table IV.

CDRs with PI-RADS stratification. Stratified analysis by PI-RADS category revealed that the diagnostic advantage of TP biopsy was most prominent in patients with a PI-RADS score of 3. In the PI-RADS 3 subgroup (n=55), the overall CDR was 3.70% (1/27) in the TR group vs. 46.43% (13/28) in the TP group (OR, 22.533; 95% CI, 2.675-189.789; P=0.0009). The detection rate of csPCa (defined as ISUP Grade Group ≥2) was also markedly higher in the TP group, at 64.29% (18/28), compared with 3.70% (1/27) in the TR group (OR, 46.800; 95% CI, 5.497-398.440, P<0.0001) (Table V). For the PI-RADS 4 group (n=72), the csPCa remained significantly higher in the TP group (72.97%; 27/37) compared with that in the TR group (31.43%; 11/35) (OR, 5.891; 95% CI, 2.129-16.299; P=0.0010), although the overall CDR exhibited no statistical difference (62.16 vs. 45.71%; P=0.2447) (Table V).

Multivariate logistic regression analysis. Univariate logistic regression was first performed to screen potential factors, and variables with P<0.2 were included as candidate variables in the multivariate analysis. Subsequently, multivariate logistic regression analysis was performed using a bidirectional stepwise selection method to identify independent factors influencing PCa detection (Table VI). The final multivariate model included biopsy group (TP vs. TR), PI-RADS category, and PSA level as covariates. Diabetes mellitus was also entered as a candidate variable as its univariate P-value was <0.2, but it was not retained in the final stepwise multivariate model. After adjustment, compared with TP biopsy as the reference, TR biopsy was associated with a lower probability of PCa detection (OR, 0.26; 95% CI, 0.11-0.58; P=0.001), while PI-RADS 4 category was associated with an increased probability of PCa detection (OR, 3.31; 95% CI, 1.44-7.57; P=0.005). PSA level showed a non-significant trend with PCa detection (OR, 1.03; 95% CI, 1.00-1.06; P=0.072).

Discussion

The primary finding of the present study was the significantly higher CDR associated with the TP biopsy technique compared with that of the TR approach. This observed difference may be related to the improved anatomical accessibility and imaging guidance associated with the TP approach. The TP approach allows for more comprehensive sampling of the prostate, especially the anterior and apical regions, which are less accessible during TR biopsies (21). This broader access

Table V. Comparison of prostate CDR between TP and TR groups with PI-RADS stratified analysis.

Analysis level	TR n/total n (%)	TP n/total n (%)	OR (95% CI)	P-value
Overall analysis				
CDR	17/62 (27.42)	36/65 (55.38)	3.286 (1.565-6.901)	0.0026
csPCa	12/62 (19.35)	45/65 (69.23)	9.375 (4.124-21.312)	<0.0001
PI-RADS=3 (n=55)				
CDR	1/27 (3.70)	13/28 (46.43)	22.533 (2.675-189.789)	0.0009
csPCa	1/27 (3.70)	18/28 (64.29)	46.800 (5.497-398.440)	<0.0001
PI-RADS=4 (n=72)				
CDR	16/35 (45.71)	23/37 (62.16)	1.951 (0.762-4.994)	0.2447
csPCa	11/35 (31.43)	27/37 (72.97)	5.891 (2.129-16.299)	0.0010

CDR, cancer detection rate; PI-RADS, Prostate Imaging Reporting and Data System; TP, transperineal; TR, transrectal; OR, odds ratio; CI, confidence interval; csPCa, clinically significant PCa.

may facilitate the identification of malignant lesions that might otherwise remain undetected, which could contribute to a higher observed CDR (22). Despite a high rate of abnormal DRE findings in both groups (>95%), the CDR in the TR group was only 27.42%. This discrepancy suggests that DRE alone may have limited predictive value, particularly when not combined with imaging. It may also reflect the reduced sensitivity of TR biopsy in detecting tumors in certain regions, such as the anterior prostate.

Additionally, the use of high-frequency ultrasound transducers in the TP approach may have contributed to the improved detection rates. High-frequency probes provide superior resolution and clarity of the prostate tissue, particularly in the anterior and apical zones, where significant carcinomas can be located but are often under-sampled by conventional TR biopsies (23-26). The enhanced visualization afforded by high-frequency imaging could facilitate more accurate targeting of suspicious areas, leading to a higher yield of positive biopsy cores (27,28). This technological advantage, together with improved anatomical accessibility of the TP route, may partially account for the higher detection rates observed in the TP group in the present study (15,24).

Anatomically, the prostate was positioned such that the TP route provides a direct path to regions that might harbor significant carcinomas yet remain unsampled in standard TR biopsies (29). Particularly, the anterior horns and the apex of the prostate, which were prone to under-sampling in TR biopsies, were more accessible via the TP route (30). Supporting this, prior research has highlighted the enhanced value of anterior sampling via the TP approach in both initial and repeat biopsies, improving the detection of clinically significant cancers in these often-overlooked regions (31). Moreover, the observed differences in the rate of abnormal biopsy results between the two methods may also be influenced by the inherent differences in patient anatomy and the nature of lesion distribution in prostate tissue (32). Anterior prostate tumors are commonly located in the anterior fibromuscular stroma and transition zone, regions that are relatively difficult to access adequately through the transrectal route. By contrast, the transperineal route provides a more direct needle trajectory to the anterior and apical regions, thereby improving sampling coverage of lesions that may be under-sampled during transrectal biopsy (33). Anterior tumors, mainly located in the anterior fibromuscular stroma and transition zone, have been reported in some studies to be associated with higher Gleason scores and more aggressive pathological features (34).

In terms of patient safety and procedural complications, the present study found no significant difference in the occurrence of adverse reactions between the two techniques, such as fever, infection and rectal bleeding. While the TR method's proximity to the bowel raises concerns regarding potential bacterial infection leading to sepsis, the rigorous use of prophylactic antibiotics in both procedures likely mitigated this risk, as evidenced by the absence of febrile complications in the present cohort (35). Nevertheless, TP biopsies have been reported to be associated with a lower risk of rectal injury and infection in a previous study (36). The present findings support this notion, showing a low incidence of rectal bleeding exclusively in the TR group, although the difference was not statistically significant.

Notably, a significantly lower urinary pH was observed in the TP group in the present study. However, this finding should be interpreted as exploratory, as the present retrospective data cannot determine whether urinary pH is directly associated with PCa detection. Urinary pH may be influenced by multiple factors, including dietary habits, renal function, urinary tract conditions and metabolic status (37); therefore, further studies are needed to clarify its potential clinical relevance.

The higher detection rates associated with the TP approach come with a need for further exploration into whether these attribute to superior prognostic outcomes and reduced mortality in patients with PCa. Given the potential for detecting clinically significant cancers that may be missed by traditional approaches, the TP biopsy approach may offer potential advantages, particularly in patients with prior negative biopsies who have persistent clinical suspicion or lesions identified to have an elevated risk on MRI (38). Furthermore, it is important to highlight the advantages of the TP biopsy technique in patients with a PI-RADS score of 3. In this specific subgroup, the TP approach offers enhanced detection

Table VI. Univariate and multivariate logistic regression analyses of factors associated with prostate cancer detection in magnetic resonance imaging-guided prostate biopsy.

	Univariate analysis					Multivariate analysis				
Parameters	β	S.E	Z	P-value	OR (95% CI)	β	S.E	Z	P-value	OR (95% CI)
Biopsy group										
TP	-	-	-	-	1.00 (Ref.)	-	-	-	-	1.00 (Ref.)
TR	-1.19	0.38	-3.14	0.002	0.30 (0.14-0.64)	-1.36	0.41	-3.29	0.001	0.26 (0.11-0.58)
PI-RADS category										
3	-	-	-	-	1.00 (Ref.)	-	-	-	-	1.00 (Ref.)
4	1.24	0.39	3.19	0.001	3.46 (1.61-7.43)	1.20	0.42	2.83	0.005	3.31 (1.44-7.57)
PSA (ng/ml)	0.03	0.01	2.31	0.021	1.03 (1.01-1.06)	0.03	0.02	1.80	0.072	1.03 (1.00-1.06)
Age (years)	0.02	0.02	0.61	0.540	1.02 (0.97-1.07)	-	-	-	-	-
BMI (kg/m^2)	-0.01	0.06	-0.21	0.834	0.99 (0.88-1.11)	-	-	-	-	-
Smoking history										
No	-	-	-	-	1.00 (Ref.)	-	-	-	-	-
Yes	-0.05	0.38	-0.14	0.891	0.95 (0.45-1.99)	-	-	-	-	-
Alcohol consumption history										
No	-	-	-	-	1.00 (Ref.)	-	-	-	-	-
Yes	-0.51	0.53	-0.97	0.334	0.60 (0.21-1.69)	-	-	-	-	-
Hypertension										
No	-	-	-	-	1.00 (Ref.)	-	-	-	-	-
Yes	-0.13	0.36	-0.35	0.729	0.88 (0.43-1.80)	-	-	-	-	-
Diabetes mellitus										
No	-	-	-	-	1.00 (Ref.)	-	-	-	-	-
Yes	1.11	0.73	1.51	0.131	3.02 (0.72-12.68)	-	-	-	-	-
Urinary pH	-0.16	0.27	-0.59	0.556	0.85 (0.50-1.46)	-	-	-	-	-
fPSA (ng/ml)	0.00	0.08	0.02	0.986	1.00 (0.85-1.17)	-	-	-	-	-

Variables with univariate P<0.2 were entered as candidate variables for multivariate analysis. Diabetes mellitus was included as a candidate variable but was not retained in the final bidirectional stepwise model. The final model included biopsy group, PI-RADS category and PSA level. PI-RADS, Prostate Imaging Reporting and Data System; TP, transperineal; TR, transrectal; OR, odds ratio; CI, confidence interval; fPSA, free prostate-specific antigen; BMI, body mass index.

capabilities due to its ability to sample difficult-to-reach areas such as the anterior and apical regions of the prostate. These areas are often under-sampled in TR biopsies but can harbor clinically significant cancers. By ensuring comprehensive coverage of all potential cancer sites, TP biopsies may help reduce sampling errors and increase the likelihood of detecting clinically significant cancers in these regions. This is particularly beneficial for patients with intermediate-risk lesions who require thorough evaluation to avoid missing significant malignancies.

Furthermore, the present study highlights the continued need for personalized medicinal approaches in PCa diagnostics. While the TP approach was associated with higher detection metrics in the present study, selection of the biopsy approach should remain guided by patient-specific anatomical, clinical and risk factors, including PSA levels, MRI findings and patient comorbidities.

Recent prospective evidence suggests that pre-biopsy conditions may also influence biopsy-related outcomes and should be considered when interpreting cancer detection results. For example, Baba *et al* (39) conducted a prospective comparative study demonstrating that ejaculation prior to prostate biopsy can alter PSA-related parameters and may affect biopsy interpretation and cancer detection outcomes, highlighting the role of patient-related pre-biopsy factors beyond imaging and biopsy route alone. These findings place the present results within a broader diagnostic context, underscoring that cancer detection is influenced by a combination of biopsy technique, imaging guidance and pre-biopsy patient conditions.

Healthcare providers might consider patient comfort and acceptable recovery times as pivotal criteria in method selection. Although not a focus of the present study, anecdotal evidence suggests TP biopsies may involve increased discomfort or a longer procedure time, which could influence patient experience.

From an economic standpoint, TP biopsy may be associated with increased resource utilization, as it sometimes involves more extended preparation, specialized equipment and longer procedure times compared with the TR approach (40). Given the absence of formal cost accounting

data in the present study, no definitive conclusions regarding economic feasibility can be drawn, and cost-related considerations should be interpreted cautiously. Future studies incorporating standardized cost analyses are warranted to better evaluate the economic implications of TP biopsy in different clinical settings (41).

Finally, it is essential to consider the implications of the present findings in the context of emerging technologies and techniques, such as MRI-ultrasound fusion-guided biopsies and advanced imaging modalities. These innovations hold promise for enhancing both TR and TP approaches by fostering greater accuracy in targeting suspicious lesions and potentially reducing the number of necessary biopsy cores, thus minimizing patient discomfort and procedural risk. In light of recent advances, the role of molecular imaging such as prostate-specific membrane antigen (PSMA) positron emission tomography/computed tomography (PET/CT) has gained attention in PCa diagnostics. Particularly, Gallium-68 PSMA PET/CT has demonstrated promising value in identifying suspicious lesions with high specificity and guiding targeted biopsy cores based on maximum standardized uptake value thresholds. This technique may be especially useful in cases with ambiguous MRI findings or recurrent negative biopsies, potentially improving the detection of clinically significant cancers while minimizing unnecessary sampling (42).

The present study has several limitations. First, its retrospective, single-center design may introduce selection bias and limit the generalizability of the findings. In addition, the non-randomized nature of the study and the protocol transition from TR to TP during the study period may have introduced time-related biases, including potential learning-curve effects as operators gained experience with targeted biopsy techniques during the TP implementation phase. Although baseline characteristics were comparable between groups, operator-related variability in biopsy technique was not fully controlled, which may have influenced diagnostic outcomes. Furthermore, the TP and TR protocols differed in several aspects beyond biopsy route (including core number, imaging modality and targeting strategy), which may confound the independent effect of biopsy route on cancer detection. Although propensity score matching might have further reduced confounding, it was not performed due to the limited sample size and the potential loss of statistical power after matching. Instead, multivariate logistic regression analysis was used to adjust for relevant covariates. Prospective randomized studies are therefore needed to better isolate the contribution of biopsy route. Another limitation is that the TR biopsy was performed without local anesthesia or analgesia, which may have affected patient comfort and tolerability. This reflects the standardized clinical practice at Anqing Municipal Hospital during the earlier phase of the study period, when TR biopsy was routinely performed without anesthesia in a real-world setting. With the subsequent adoption of TP biopsy, local anesthesia protocols were implemented in line with evolving patient-centered care practices. As pain and patient-reported outcomes were not predefined study endpoints, anesthesia strategies were not controlled in this retrospective cohort. Although pain assessment was not a primary endpoint of this study, the absence of anesthesia does not fully align with current patient-centered clinical practice and may limit the generalizability of the TR group's safety profile. Future studies should standardize anesthesia protocols and incorporate patient-reported pain outcomes. In addition, the observed difference in urinary pH between groups should be interpreted cautiously. As this retrospective study did not include preoperative dietary questionnaires or detailed renal function indicators (such as urine specific gravity or creatinine clearance), the biological mechanisms underlying this finding could not be adequately explored. Urinary pH should therefore be regarded as an exploratory observation with uncertain clinical relevance. Future studies incorporating dietary assessment and comprehensive renal function evaluation are needed to determine whether urinary biochemical characteristics are associated with PCa detection or biopsy outcomes. All patients received a 5-day course of broad-spectrum antibiotics (ciprofloxacin plus metronidazole) after biopsy according to the institutional protocol, which reflects local antibiotic resistance patterns, including a high prevalence of fluoroquinolone-resistant *Escherichia coli*. While this regimen may have contributed to the low infection rate observed, it may limit the generalizability of infection-related findings to settings using shorter antibiotic courses or with different resistance profiles. Future studies could explore tailored antibiotic prophylaxis strategies based on regional resistance data.

In conclusion, in the present retrospective single-center study, the TP protocol used in Anqing Municipal Hospital was associated with a higher cancer detection rate than the TR protocol, with similar safety outcomes. Given the non-randomized design and protocol differences between groups, these findings should be interpreted cautiously and warrant confirmation in prospective multicenter studies with standardized imaging and sampling schemes.

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Availability of data and materials

The data generated in the present study may be requested from the corresponding author.

Authors' contributions

JZ was responsible for conceptualization, methodology, data curation, formal analysis, writing the original manuscript draft and visualization. HZ was responsible for conceptualization, methodology, supervision, project administration, resources, critical revisions for important intellectual content, and validation. JZ and HZ confirm the authenticity of all the raw data. Both authors have read and approved the final version of the manuscript, have agreed on the journal to which the article has been submitted and have agreed to be accountable for all aspects of the work.

Ethics approval and consent to participate

This study was conducted in compliance with the Declaration of Helsinki. Approval for the study was received from the Institutional Review Board and Ethics Committee of Anqing Municipal Hospital [Anqing, China; approval no. Medical Ethics Review (2025) no. 54]. The requirement for written informed consent was waived due to the retrospective nature of the study, as it involved only de-identified patient data and posed no risk or impact on patient care. The waiver was granted in compliance with regulatory and ethical guidelines relevant to retrospective research studies.

Patient consent for publication

Not appliable.

Competing interests

The authors declare that they have no competing interests.

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