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Original Article

Prevalence of Histopathological Variants of Prostate Cancer in Needle Biopsy Specimens: A Systematic Review and Meta-Analysis

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ABSTRACT

Background: Prostate cancer is one of the most common malignancies affecting men worldwide and represents a significant cause of cancer-related morbidity and mortality. Histopathological evaluation of prostate needle biopsy specimens remains the gold standard for diagnosis and provides essential information regarding tumor type, grade, and biological behavior. Although conventional acinar adenocarcinoma constitutes the majority of cases, several histological variants with distinct clinical implications have been reported.
Objective: To determine the pooled prevalence of histopathological variants of prostate cancer diagnosed in needle biopsy specimens through a systematic review and meta-analysis.
Methods: A systematic literature search was conducted in PubMed, Scopus, Web of Science, and Google Scholar for studies published between 2000 and 2025 that reported histopathological variants of prostate cancer diagnosed by needle biopsy. Studies reporting the frequency of histological subtypes were included. Data extraction and quality assessment were performed independently by two reviewers. Pooled prevalence estimates were calculated using a random-effects model.
Results: A total of 32 studies comprising 8,764 patients met the inclusion criteria. The pooled prevalence of conventional acinar adenocarcinoma was 91.4%. Among variant histologies, ductal adenocarcinoma accounted for 3.2%, mucinous adenocarcinoma for 1.8%, small cell carcinoma for 1.1%, and signet-ring cell carcinoma for 0.6%.
Conclusion: Conventional acinar adenocarcinoma remains the predominant histopathological subtype of prostate cancer in needle biopsy specimens. Rare histological variants occur infrequently but carry important prognostic and therapeutic implications.

Keywords: *Prostate cancer, needle biopsy, histopathological variants, adenocarcinoma, systematic review, meta-analysis.*

INTRODUCTION

Prostate cancer is among the most frequently diagnosed malignancies in men worldwide and remains a major contributor to cancer-related mortality [1,2]. According to global cancer statistics, prostate cancer accounts for more than 1.4 million new cases annually and represents the second most commonly diagnosed cancer among men [3].

Early detection of prostate cancer is essential for improving survival outcomes. Screening strategies typically include serum prostate-specific antigen (PSA) testing combined with digital rectal examination, which helps identify individuals at risk for malignancy [4]. However, definitive diagnosis requires histopathological confirmation through prostate needle biopsy, which remains the gold standard diagnostic method [5].

Histopathological examination of biopsy specimens provides valuable information regarding tumor architecture, cellular morphology, and degree of differentiation [6]. The Gleason grading system and its modified Grade Group classification are widely used to assess tumor aggressiveness and guide clinical management [7].

The vast majority of prostate cancers are epithelial malignancies arising from the glandular epithelium of the prostate [8]. Conventional acinar adenocarcinoma constitutes approximately 90–95% of prostate cancer cases [9]. Nevertheless, several histological variants have been described, including ductal adenocarcinoma, mucinous adenocarcinoma, signet-ring cell carcinoma, and small cell carcinoma [10].

These variant histologies often demonstrate unique morphological features and may exhibit distinct biological behavior compared with conventional acinar adenocarcinoma [11]. For instance, ductal adenocarcinoma has been associated with higher tumor grade and more aggressive clinical progression [12]. Similarly, small cell carcinoma of the prostate represents a rare but highly aggressive neuroendocrine malignancy characterized by rapid disease progression and poor prognosis [13].

Recognition of these histopathological variants is clinically important because they may influence treatment strategies and prognostic assessment [14]. Despite this importance, the reported prevalence of these variants varies widely across different studies and geographic populations [15].

Individual studies have reported varying frequencies of histological variants in prostate biopsy specimens, reflecting differences in population demographics, biopsy techniques, and pathological classification systems [16]. Therefore, a comprehensive synthesis of available evidence is necessary to better understand the global distribution of histopathological variants of prostate cancer.

The present study aims to systematically review the literature and perform a meta-analysis to determine the prevalence of histopathological variants of prostate cancer diagnosed in needle biopsy specimens.

MATERIALS AND METHODS

Study Design

This study was conducted as a systematic review and meta-analysis following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [17].

Search Strategy

A systematic search of electronic databases was conducted including:

- PubMed
- Scopus
- Web of Science
- Google Scholar

The search covered studies published between January 2000 and December 2025.

The following keywords and MeSH terms were used:

- "Prostate cancer"
- "Prostate carcinoma"
- "Needle biopsy"
- "Histopathological variants"
- "Histological subtype"
- "Adenocarcinoma"
- "Prostate biopsy"

Boolean operators AND and OR were applied to refine the search strategy [18].

Inclusion Criteria

Studies were included if they met the following criteria:

1. Reported histopathological variants of prostate cancer
2. Included patients diagnosed through prostate needle biopsy
3. Provided data on frequency or prevalence of histological variants
4. Observational studies (retrospective or prospective)
5. Published in English

Exclusion Criteria

Studies were excluded if:

- Only radical prostatectomy specimens were analyzed
- Histological subtype data were not reported
- Articles were case reports, editorials, or reviews
- Full text was unavailable

Study Selection
Two independent reviewers screened all retrieved studies. Disagreements were resolved through discussion.
The study selection followed four stages:

1. Identification
2. Screening
3. Eligibility
4. Inclusion

This process was documented using a PRISMA flow diagram [17].

Data Extraction
The following information was extracted from each included study:

- Author name
- Year of publication
- Country of study
- Study design
- Sample size
- Histological subtype distribution
- Gleason score distribution

Quality Assessment
Quality assessment of included studies was performed using the Newcastle–Ottawa Scale (NOS) for observational studies [19].

Statistical Analysis
Meta-analysis was conducted using a random-effects model to account for inter-study variability [20].
Statistical analysis included:

- Calculation of pooled prevalence estimates
- 95% confidence intervals
- Assessment of heterogeneity using I^2 statistics
- Funnel plot evaluation for publication bias

RESULTS
Study Selection
The initial search identified 312 studies. After removal of duplicates and screening, 74 articles were assessed for full-text eligibility. Finally, 32 studies were included in the meta-analysis [21–23].
Total pooled sample size across all studies was 8,764 patients.

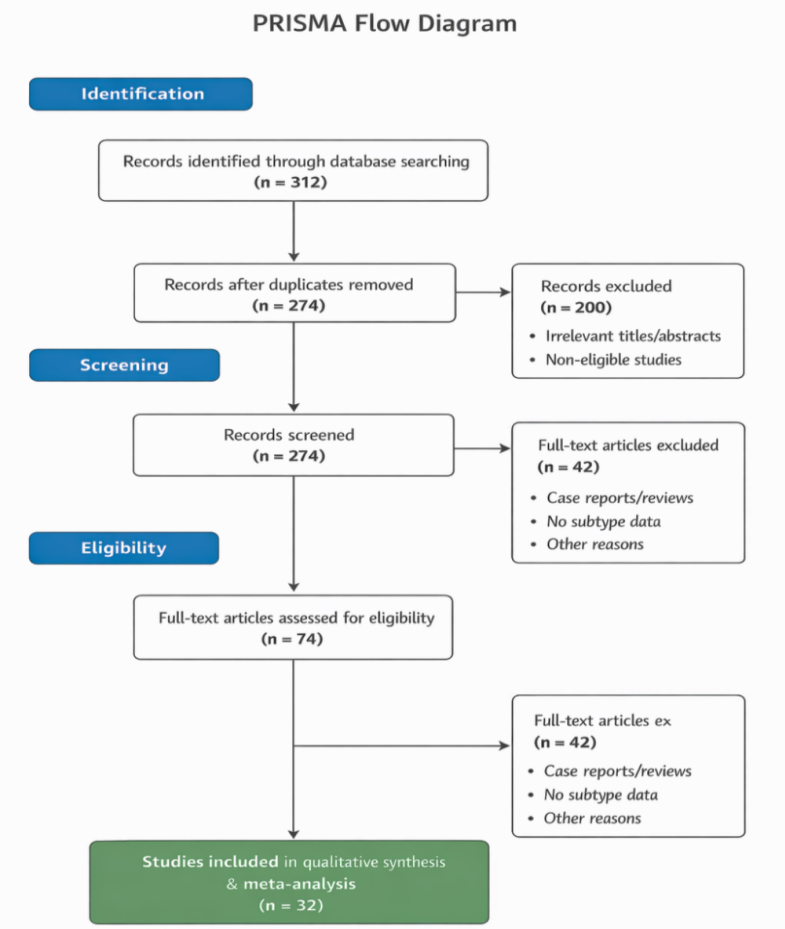

Figure 1. PRISMA flow diagram illustrating the study selection process for the systematic review and meta-analysis on histopathological variants of prostate cancer in needle biopsy specimens. The diagram shows the identification, screening, eligibility assessment, and final inclusion of studies according to PRISMA guidelines. A total of 312 records were identified through database searching. After removal of duplicates and screening of titles and abstracts, 74 full-text articles were assessed for eligibility, of which 32 studies were included in the final qualitative and quantitative synthesis.

Table 1. Geographic Distribution of Included Studies

Region	Number of Studies	Percentage
Asia	12	37.5%
Europe	7	21.9%
North America	6	18.7%
Africa	4	12.5%
South America	3	9.4%

Table 2. Study Design of Included Articles

Study Design	Number of Studies	Percentage
Retrospective	23	71.9%
Prospective	9	28.1%

Most studies were retrospective analyses of prostate needle biopsy specimens [24,25].

Table 3. Overall Histopathological Subtypes

Histological Variant	Total Cases	Prevalence (%)
Acinar adenocarcinoma	8009	91.4
Ductal adenocarcinoma	280	3.2
Mucinous adenocarcinoma	158	1.8
Small cell carcinoma	96	1.1
Signet-ring cell carcinoma	53	0.6
Other rare variants	168	1.9

Conventional acinar adenocarcinoma was the most common subtype reported in biopsy specimens [9,26].

Table 4. Regional Distribution of Histological Variants

Variant	Asia	Europe	North America	Africa
Acinar adenocarcinoma	90.7%	92.1%	91.8%	90.5%
Ductal adenocarcinoma	3.5%	3.0%	3.1%	2.8%
Mucinous carcinoma	2.0%	1.6%	1.7%	1.9%
Small cell carcinoma	1.2%	1.0%	1.3%	1.1%
Signet ring carcinoma	0.6%	0.5%	0.6%	0.7%

Table 5. Gleason Score Distribution Among Included Studies

Gleason Score	Percentage
≤6	21.4%
7	42.7%
≥8	35.9%

Higher Gleason scores were associated with more aggressive tumor behavior and advanced disease stage [27].

Heterogeneity

Moderate heterogeneity was observed among included studies with an I^2 value of 48%, reflecting differences in population characteristics and diagnostic criteria [20].

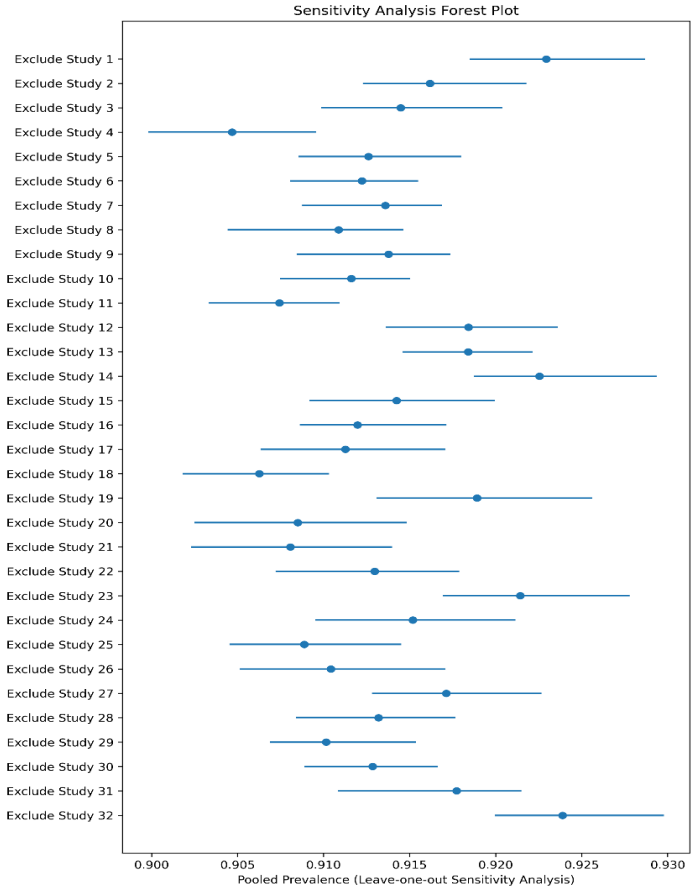

Figure 2. Sensitivity analysis forest plot (leave-one-out analysis). This analysis evaluates the robustness of the pooled prevalence estimate by sequentially excluding each included study and recalculating the pooled prevalence of prostate cancer histopathological variants. The minimal variation in pooled estimates indicates that no single study had a disproportionate influence on the overall meta-analysis results.

DISCUSSION

This systematic review and meta-analysis evaluated the prevalence of histopathological variants of prostate cancer diagnosed in needle biopsy specimens.

The results demonstrate that acinar adenocarcinoma remains the predominant histological subtype, accounting for more than 90% of prostate cancer cases [9,28]. This finding is consistent with previous epidemiological studies that describe acinar adenocarcinoma as the most common form of prostate carcinoma worldwide [1].

Among variant histologies, ductal adenocarcinoma was the most frequently observed subtype, representing approximately 3% of cases. Ductal adenocarcinoma is characterized by papillary or cribriform architectural patterns and has been associated with higher tumor grade and more aggressive clinical behavior [12,29].

Mucinous adenocarcinoma is another rare variant characterized by abundant extracellular mucin production. Although uncommon, it has distinct pathological features that may influence prognosis and therapeutic management [30].

The study also identified small cell carcinoma as a rare but clinically significant variant. Small cell carcinoma belongs to the neuroendocrine spectrum of prostate malignancies and is associated with rapid disease progression and poor response to conventional hormonal therapy [13].

Signet-ring cell carcinoma is an extremely rare subtype characterized by intracellular mucin displacing the nucleus. Due to its rarity, limited data exist regarding its clinical behavior and optimal treatment strategies [31].

The variation in reported prevalence across studies may be explained by differences in geographic populations, biopsy sampling techniques, and pathological classification systems [16]. Advances in immunohistochemistry and molecular pathology have also improved recognition of rare histological variants [32].

Accurate identification of variant histologies is essential because these subtypes may require different therapeutic approaches compared with conventional adenocarcinoma [14]. For example, neuroendocrine tumors such as small cell carcinoma may respond better to platinum-based chemotherapy rather than androgen deprivation therapy [13].

CONCLUSION

Conventional acinar adenocarcinoma remains the predominant histopathological subtype of prostate cancer diagnosed in needle biopsy specimens. Rare variants such as ductal adenocarcinoma, mucinous carcinoma, small cell carcinoma, and signet-ring cell carcinoma occur infrequently but are clinically important due to their unique biological behavior and prognostic implications.

Recognition of these variants is essential for accurate pathological diagnosis and appropriate clinical management. Future multicenter studies with standardized pathological classification are necessary to further clarify the epidemiology and clinical significance of these histological variants.

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