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The prognostic value of zonal origin in clinically localized prostate cancer: a systematic review and meta-analysis

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Jin, SJ[1]; Wu, LY[2]; Liang, Z[3]; Yan, WG[4].

Corresponding author:
Shijie Jin

jinshijie_pumc@sina.com

Author Affiliation:
Peking Union Medical College.

ADMINISTRATIVE INFORMATION

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 25 November 2023 and was last updated on 25 November 2023.

INTRODUCTION

Review question / Objective P: Patients who were diagnosed with clinically localized prostate cancer. I/C: The zonal origin of prostate cancer: peripheral zone or transition zone. O: Biochemical recurrence after prostatectomy or radiation therapy. S: RCT, cohort studies, and case-control studies.

Rationale Prostate cancer (PC) is the second most common cancer in men and the sixth most common cause of cancer death worldwide in 2020, causing >350,000 deaths in men. The human prostate was histologically divided into transition zone (TZ), peripheral zone (PZ), central zone (CZ), and anterior fibromuscular stroma (AFMS) by McNeal. Approximately 25%, 70%, and 5% of prostate cancer originate respectively from TZ, PZ, and CZ. Compared with PZ tumors, most TZ tumors are usually diagnosed with larger volume and higher prostatic specific antigen (PSA) levels, but with earlier T stage and lower Gleason scores, indicating that TZ tumors might have better biological behavior. Some studies suggested that zonal origin in TZ was associated with a lower risk of BCR. Conversely, other studies found no significant differences in 5-year biochemical relapse-free survival between TZ tumors and PZ tumors. Therefore, the prognostic role of zonal origin in prostate cancer is still controversial. We aim to conduct a meta-analysis of all eligible published studies to quantify the prognostic value of zonal origin in prostate cancer.

Condition being studied Patients with clinically localized prostate cancer.

METHODS

Search strategy We conducted this meta-analysis according to the Meta-analysis of Observational Studies in Epidemiology (MOOSE) guidelines and Preferred Reporting Items for Systematic Reviews

and Meta-analysis (PRISMA) guidelines. The Medline, Embase, Scopus, Web of Science, and Cochrane databases were searched from inception to November 1st, 2022 for human studies investigating the association between zonal origin and BCR in prostate cancer. The main search terms included: (zone or zonal) and (prostate or prostatic) and (cancer carcinoma) and (recurrence or failure or relapse). The reference lists of retrieved articles were also checked for relevant articles.

Participant or population Patients with clinically localized prostate cancer who receive prostatectomy or radiation therapy.

Intervention Prostate cancer originating from the transition zone.

Comparator Prostate cancer originating from the peripheral zone.

Study designs to be included RCT, cohort studies, and case-control studies.

Eligibility criteria Inclusion criteria for selecting the studies were as follows: (i) The diagnosis of prostate cancer was pathologically confirmed; (ii) Zonal origin was defined as the zone which contains most part of the index tumor with the highest Gleason score; (iii) Correlation of zonal origin with BCR was reported.

Information sources The Medline, Embase, Scopus, Web of Science, and Cochrane databases.

Main outcome(s) HR, RR, or OR evaluating the risk of biochemical recurrence, together with their 95% CI.

Additional outcome(s) Authors, year of publication, country, the proportion of different ethnic groups, study design, number of cases, treatment, follow-up time, the definition of zonal origin, and the definition of biochemical recurrence.

Quality assessment / Risk of bias analysis The Newcastle–Ottawa Scale (NOS) (range 1–9 scores) was used(16). NOS scores of ≥8 were defined as high-quality studies.

Strategy of data synthesis We pooled RRs and 95% CIs using random-effects models and fixed-effects models according to the heterogeneity evaluated by Cochran's Q test and Higgins I-squared statistic. An $I2 > 50\%$ was considered as significant heterogeneity and a random-effect model (DerSimonian–Laird method) was used. Otherwise, the fixed-effects model (Mantel–Haenszel method) was adopted.

Subgroup analysis A subgroup analysis was performed based on variables including major ethnic group, sample size, median follow-up time, regression model type (univariate or multivariate), RR source (direct extraction or indirect estimate), NOS total score, the definition of BCR, the definition of TZ origin (on MRI or pathological sections), pre-treatment PSA level, the ratio of Gleason grade group ≥2, and the ratio of T stage ≥T3.

Sensitivity analysis Sensitivity analysis was conducted by omitting one study at a time, generating the pooled estimates, and comparing them with the original estimates.

Language restriction English.

Country(ies) involved China.

Keywords prostatic neoplasms, transition zone, peripheral zone, prognosis, biochemical recurrence.

Contributions of each author
Author 1 - Shijie Jin.
Author 2 - Liyi Wu.
Author 3 - Zhen Liang.
Author 4 - Weigang Yan.