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Wang, Q¹; Ketteler, S²; Bagheri, S³; Ebrahimifard, A⁴; Luster, M⁵; Librizzi, D⁶; Yousefi, BH⁷.**ADMINISTRATIVE INFORMATION****Support** - CSC(No.202208140021).**Review Stage at time of this submission** - Data extraction.**Conflicts of interest** - None declared.**INPLASY registration number:** INPLASY202420065**Amendments** - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 15 February 2024 and was last updated on 15 February 2024.**INTRODUCTION**

Review question / Objective Prompt and accurate diagnosis of prostate cancer (PCa) is of paramount importance for effective treatment planning. While Gallium-68 labeled prostate-specific membrane antigen (PSMA) positron emission tomography (PET)/computed tomography (CT) has proven efficacy in detecting PCa, limited availability poses challenges. As a potential alternative, [99mTc]Tc-PSMA single photon emission computed tomography (SPECT)/computed tomography (CT) holds promise. The purpose of this study is to evaluate the diagnostic value of [99mTc]Tc-PSMA SPECT/CT for prostate cancer.

P: Patients with suspected prostate cancer or patients with prostate cancer;

I: [99mTc]Tc-PSMA SPECT/CT;

C: Histopathology, imaging, or clinical follow-up;

O: Diagnostic accuracy;

S: RCT, or cohort study, or case-control study.

Condition being studied Early diagnosis is very important in the treatment of prostate cancer(PCa). Gallium-68 labeled prostate-specific membrane antigen(PSMA) PET/CT has a well-established role in detecting PCa patients. However, limited PET/CT facilities and an insufficient supply of 68Ga-PSMA make it more challenging to deliver this highly valuable diagnostic test to patients. Technetium-99m labeled PSMA ligands and more readily available scanner SPECT/CT may be potential alternatives to 68Ga-PSMA PET/CT. However, only a few studies have evaluated the role of 99mTc-PSMA SPECT/CT in the diagnosis of PCa. Previous literature has reported the diagnostic efficacy of 99mTc-PSMA SPECT/CT for prostate cancer. A meta-analysis can obtain a more reliable conclusion by systematically

combining the indicators of diagnostic accuracy of included studies.

METHODS

Search strategy The search keywords were as follows: (1) "Prostatic Neoplasms" OR "Prostate Cancer"; (2) "Tomography, Emission-computed, Single-photon"; (3) "Technetium" OR "Technetium-99m" OR "Tc-99m"; (3) "Sensitivity" OR "Specificity". Take the pubmed search query as an example: (((("Prostatic Neoplasms"[Mesh]) OR (((((((((((((((Neoplasms, Prostate[Title/Abstract]) OR (Neoplasm, Prostate[Title/Abstract])) OR (Prostate Neoplasm[Title/Abstract])) OR (Neoplasms, Prostatic[Title/Abstract])) OR (Neoplasm, Prostatic[Title/Abstract])) OR (Prostatic Neoplasm[Title/Abstract])) OR (Prostate Cancer[Title/Abstract])) OR (Cancer, Prostate[Title/Abstract])) OR (Cancers, Prostate[Title/Abstract])) OR (Prostate Cancers[Title/Abstract])) OR (Cancer of the Prostate[Title/Abstract])) OR (Prostatic Cancer[Title/Abstract])) OR (Cancer, Prostatic[Title/Abstract])) OR (Cancers, Prostatic[Title/Abstract])) OR (Prostatic Cancers[Title/Abstract])) OR (Cancer of Prostate[Title/Abstract])) AND ("Tomography, Emission-Computed, Single-Photon"[Mesh]) OR (((((((((((((((CT Scan, Single-Photon Emission[Title/Abstract]) OR (CT Scan, Single Photon Emission[Title/Abstract])) OR (Radionuclide Tomography, Single-Photon Emission-Computed[Title/Abstract])) OR (Radionuclide Tomography, Single Photon Emission Computed[Title/Abstract])) OR (Tomography, Single-Photon, Emission-Computed[Title/Abstract])) OR (Single-Photon Emission Computerized Tomography[Title/Abstract])) OR (Single Photon Emission Computerized Tomography[Title/Abstract])) OR (Single-Photon Emission CT Scan[Title/Abstract])) OR (Single Photon Emission CT Scan[Title/Abstract])) OR (Single-Photon Emission-Computed Tomography[Title/Abstract])) OR (Emission-Computed Tomography, Single-Photon[Title/Abstract])) OR (Single Photon Emission Computed Tomography[Title/Abstract])) OR (Tomography, Single-Photon Emission-Computed[Title/Abstract])) OR (SPECT[Title/Abstract])) OR (CAT Scan, Single-Photon Emission[Title/Abstract])) OR (CAT Scan, Single Photon Emission[Title/Abstract])) OR (Single-Photon Emission Computer-Assisted Tomography[Title/Abstract])) OR (Single Photon Emission Computer Assisted Tomography[Title/Abstract])))) AND ("Technetium"[Mesh]) OR (((((((((((Technetium 99m[Title/Abstract]) OR (99m, Technetium[Title/Abstract])) OR (99m-Tc[Title/Abstract])) OR ((99m)Tc[Title/Abstract])) OR (99m,Tc[Title/Abstract])) OR (99m Tc[Title/

Abstract])) OR (Tc-99m[Title/Abstract])) OR (Tc(99m[Title/Abstract])) OR (Tc,99m[Title/Abstract])) OR (Tc 99m[Title/Abstract])) AND (sensitivity[Title/Abstract] OR sensitivity and specificity[MeSH Terms] OR (predictive[Title/Abstract] AND value*[Title/Abstract]) OR predictive value of tests[MeSH Terms] OR accuracy*[Title/Abstract]).

Participant or population Patients with suspected prostate cancer or patients with prostate cancer.

Intervention Image result of 99m-Tc PSMA SPECT/CT scans of patients with suspected prostate cancer or patients with prostate cancer.

Comparator Histopathology or/and imaging or clinical follow-up of patients.

Study designs to be included RCT, or cohort study, or case-control study; Prospective research and retrospective research.

Eligibility criteria Inclusion criteria: (1) [99mTc]Tc-PSMA SPECT/CT was used to diagnose prostate cancer patients; (2) Studies assessed the diagnostic sensitivity and specificity can use histopathology or/and imaging or clinical follow-up as a reference standard; (3) Patient-based research; (4) Sufficient data were presented to calculate the true-positive (TP), false-positive (FP), false-negative (FN), and true-negative (TN) values for the imaging techniques.Exclusion criteria: (1) Review or meta-analysis, case report; (2) The data provided by the article was not enough to calculate the diagnostic accuracy; (3) The research content was irrelevant to this study; (4) Publications with study population overlap; (5) Patients with a secondary malignoma were excluded from the study.

Information sources Bibliographic databases PubMed, Cochrane, EMBASE and Web of Science were searched. The search included combinations of the following terms: (1) prostate neoplasms; (2) technetium; (3) tomography, emission-computerised, single-photon; (4) sensitivity or specificity.

Main outcome(s) Diagnostic accuracy indicators, including sensitivity, specificity, diagnostic odds ratio (DOR), negative likelihood ratio, and positive likelihood ratio, will be pool. The area under the curve (AUC) of the combined model will be calculated using summary receiver-operating characteristic (SROC) curves.

Data management EndNote.

Quality assessment / Risk of bias analysis The Quality Assessment of Diagnostic Accuracy Studies (QUADAS-2) scale, which includes four domains: case selection, diagnostic tests evaluated, gold standards, and case flow and time interval between diagnostic tests and gold standards, will be used to assess the methodological quality and risk of bias of the included studies. Low, high or unclear risk will be assessed for each domain.

Strategy of data synthesis STATA 18 and MetaDisc 1.4 will be used for statistical calculations in this study. Diagnostic accuracy indicators, including sensitivity, specificity, diagnostic odds ratio (DOR), negative likelihood ratio, and positive likelihood ratio, were pooled. The combined model's area under the curve (AUC) was calculated using summary receiver-operating characteristic (SROC) curves. The heterogeneity among the included studies was quantified using Cochrane Q statistics and I² statistics. We assessed the publication bias of the included studies using Deek's funnel plot. All hypothesis tests were statistically significant with a two-sided P-value of less than 0.05.

Subgroup analysis If the literature is sufficient, subgroup analysis will be performed according to radiotracer.

Sensitivity analysis If the combined results of the remaining documents are not significantly different from those without deletion, it means that the sensitivity analysis has passed.

Language restriction English.

Country(ies) involved Germany, Iran, China.

Keywords Prostate cancer, Technetium, PSMA, SPECT/CT, Meta-analysis.

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