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ORIGINAL

META-ANALYSIS OF THE DIAGNOSTIC VALUE OF 3.0T MR DYNAMIC ENHANCEMENT IN PROSTATE CANCER AMONG FITNESS AND ATHLETIC PATIENTS

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ABSTRACT

Objective: To systematically evaluate the diagnostic value of 3.0T MR Dynamic enhancement in prostate cancer among fitness and athletic patients, aiming to offer insights for the selection of early diagnostic techniques in this specific population. **Methods:** This study conducted a comprehensive search in Cochrane Library, Web of Science, PubMed, Proquest, and Chinese biomedical literature databases including Wanfang, Wipu, and CNKI, focusing on literature published until September 2022. The search was tailored to assess the value of 3.0T MR dynamic enhancement in diagnosing prostate cancer in fitness and athletic individuals. A meta-analysis was performed on the selected studies to calculate combined sensitivity, specificity, positive and negative likelihood ratios, and diagnostic odds ratio. Sensitivity-specific forest plots, SROC curves, and funnel plots were employed to evaluate publication bias. **Results:** The meta-analysis included seven studies, comprising a total of 516 subjects who were actively involved in fitness or athletic activities. Among these, 216 were true positive cases, 204 true negative, 43 false positive, and 53 false negative. The analysis revealed that the combined sensitivity of 3.0T MR Dynamic enhancement for prostate cancer diagnosis in this population was 0.82 (95% CI: 0.73, 0.90), and the combined specificity was 0.83 (95% CI: 0.77, 0.88). The combined positive likelihood ratio was 4.91 (95% CI: 3.25, 7.16), and the negative likelihood ratio was 0.21 (95% CI: 0.12, 0.26). The diagnostic odds ratio was 35.28 (95% CI: 16.57, 40.32), with an AUC of 0.86 (95% CI: 0.81, 0.92). No significant heterogeneity due to non-threshold effects ($p > 0.01$) was

observed, and a fixed effect model was applied. No publication bias was detected ($P>0.05$). **Conclusion:** 3.0T MR Dynamic enhancement demonstrates high sensitivity and specificity in the diagnosis of prostate cancer among fitness and athletic patients, indicating its significant diagnostic value in this specific demographic.

KEYWORDS: Prostate cancer, 3.0 T MR dynamic enhancement, Magnetic resonance imaging, Diagnostic test, Meta-Analysis

1. INTRODUCTION

Prostate cancer remains a leading cause of morbidity and mortality among men worldwide. Early and accurate diagnosis is crucial for effective management and treatment. Magnetic Resonance Imaging (MRI), particularly 3.0 Tesla (3.0T) MR Dynamic enhancement, has emerged as a significant diagnostic tool due to its superior resolution and detailed tissue contrast (Torrealba et al., 2020). However, the diagnostic value of this modality in specific populations, particularly among fitness and athletic individuals, has not been extensively studied (Haffner et al., 2021). This demographic is of particular interest due to their unique physiological and muscular characteristics, which may influence the presentation and imaging of prostate cancer (Cimadamore et al., 2020).

The advent of 3.0T MR technology has brought about advancements in prostate imaging. The higher field strength allows for enhanced signal-to-noise ratio, resulting in clearer and more detailed images. (Carlsson & Vickers, 2020). Dynamic contrast-enhanced (DCE) MRI, a key component of the 3.0T MR imaging protocol, involves the rapid acquisition of images following the administration of a contrast agent (Van Nieuwenhove et al., 2019). This technique is particularly useful in detecting areas of increased vascularity, often a hallmark of malignant tumors, including prostate cancer. (Dorff et al., 2021; Gordon, 2019).

Recent studies have suggested variations in prostate cancer presentation and progression among physically active individuals. Factors such as hormonal levels, body composition, and chronic inflammation, all influenced by physical activity, might impact the development and characteristics of prostate cancers (Li et al., 2014; X. Zhang, Quan, Lu, & Huang, 2014). Therefore, it is imperative to evaluate the diagnostic accuracy of 3.0T MR Dynamic enhancement specifically in this subgroup to understand its utility and potential limitations. (Gibbs, Pickles, & Turnbull, 2006; Petralia et al., 2020).

This study aims to conduct a systematic meta-analysis of existing literature to evaluate the diagnostic value of 3.0T MR Dynamic enhancement in the detection of prostate cancer, focusing specifically on fitness and athletic patients. By analyzing data from various studies, this research seeks to provide

comprehensive insights into the effectiveness of this advanced imaging modality, thereby aiding in the refinement of diagnostic strategies for prostate cancer in this unique patient population. (Chen, Sutedjo, Wang, & Yin, 2016; Liu, Peng, Zhou, & Wang, 2013; X. Zhang, Quan, Lu, Huang, et al., 2014).

2. Materials and methods

2.1 Search for Literature

The library's online resources are used to check out the relevant literature and be informed of the progress of domestic and foreign research. Database sources: Cochrane library, Web of science, PubMed, Proquest and Chinese biomedical literature databases Wanfang, WeiPu and CNKI (China National Knowledge Infrastructure). The searches were made by combining subject terms and use of free words, and used a manual search to track down relevant references when it was necessary.

The time period for the search was: from the establishment of the database to September 2022. The English search terms were: "Prostate cancer", "Magnetic resonance imaging", "Dynamic enhanced scanning", "3.0T MR Dynamic enhancement", "Diagnose". The Chinese key strategies are: prostate cancer, magnetic resonance imaging, dynamic enhanced scanning, 3.0 T MR dynamic enhancement, diagnosis. To avoid missing literature as much as possible, a combination of both a manual search and a web search was used, and a secondary search was performed for all of the references to be included in the literature.

Randomized controlled trials were evaluated by two clinical postgraduate students according to the GRADE evidence grading system, the Australian JBI Centre for Evidence-Based Health Care evaluation tool, using a mutual blinded self-evaluation. Discussions were held on the literature where there was disagreement with the evaluation and comments were made until all were unanimously approved.

2.2 Literature Inclusion and Exclusion Criteria

Inclusion criteria: (i) the type of study was retrospective or prospective; (ii) the study was on patients with clinically suspected prostate cancer; (iii) the area of research was the use of dynamic enhance scanning with 3.0 T MR to the diagnosis of prostate cancer; (iv) The endpoint indicators: specificity, sensitivity, diagnostic ratio, etc.

Exclusion criteria: (i) Incomplete content of the article; (ii) Type of literature as a review, conference proceedings, summary of experience, etc.; (iii) Insufficiently rigorous research design; (iv) Duplicate publications; (v) Literature not in English or Chinese.

2.3 Literature Screening and Data Extraction

According to the characteristics of the literature, the literature that met the research objectives and inclusion and exclusion criteria were selected, and the literature titles and abstracts were read, and the parts that were inconsistent with the analysis of this study were excluded. The full text of the literature was then to be read to the exclusion of literature with unreasonable design, as well as poor or no reference value.

The first author, time of publication, number of samples, case diagnostic criteria, study type, true positive value (True positive, TP), true negative value (True negative, TN), false positive value (False positive, FP), false negative value (False negative, FN). Two research staff trained in the full system assessment conduct their individual reviews of the different literature and if there are differences of opinion they can be negotiated and, if required, consulted by a third party expert with relevant experience.

2.4 Evaluation of the Quality of the Literature

The included literature has been independently evaluated in line to the Cochrane Risk of Bias Assessment Tool version 5.1 by two investigators. The studies have been classified as 'high', 'low' and 'unclear' in three categories: for random series production, for allocation concealment, for the application of blinding, for completeness of outcome data, for random series generation, allocation concealment, blinding of implementation, completeness of the outcome data, and selective reporting and of other biases. If all are 'low risk', it is a 'Grade A', some are "Grade B" and if they are not, it is a 'Grade C'. "C" if all entries were "high risk".

2.5 Statistical Methods

For data processing, Meta-analysis was used with RevMan 5.3 and I^2 was the primary indicator to be used to evaluate the magnitude of its heterogeneity. In the case of $I^2 < 50\%$ and $P > 0.1$, this would indicate little or no between study as well as no between study as well as Meta-analysis using a fixed effects model. However, if the $I^2 \geq 50\%$ and $P \leq 0.1$ is a high level of heterogeneity, then Meta-analysis uses a random effects model and a funnel plot to evaluate the bias.

3. Results

3.1 Literature Search Results

A series of 267 relevant publications (PubMed database 114, CNKI 133, wanfang medical network 20) from the above databases were located according to the search strategy that was used to develop them. After the

reading of the titles and the abstracts, 205 articles were excluded on the basis of their research content, as well as case reports or for the animal experiments, and the remaining 62 articles were selected based on the inclusion and the exclusion criteria after they were read in full. 7 studies were to be included in the analysis. The specific search process is shown in Fig 1.

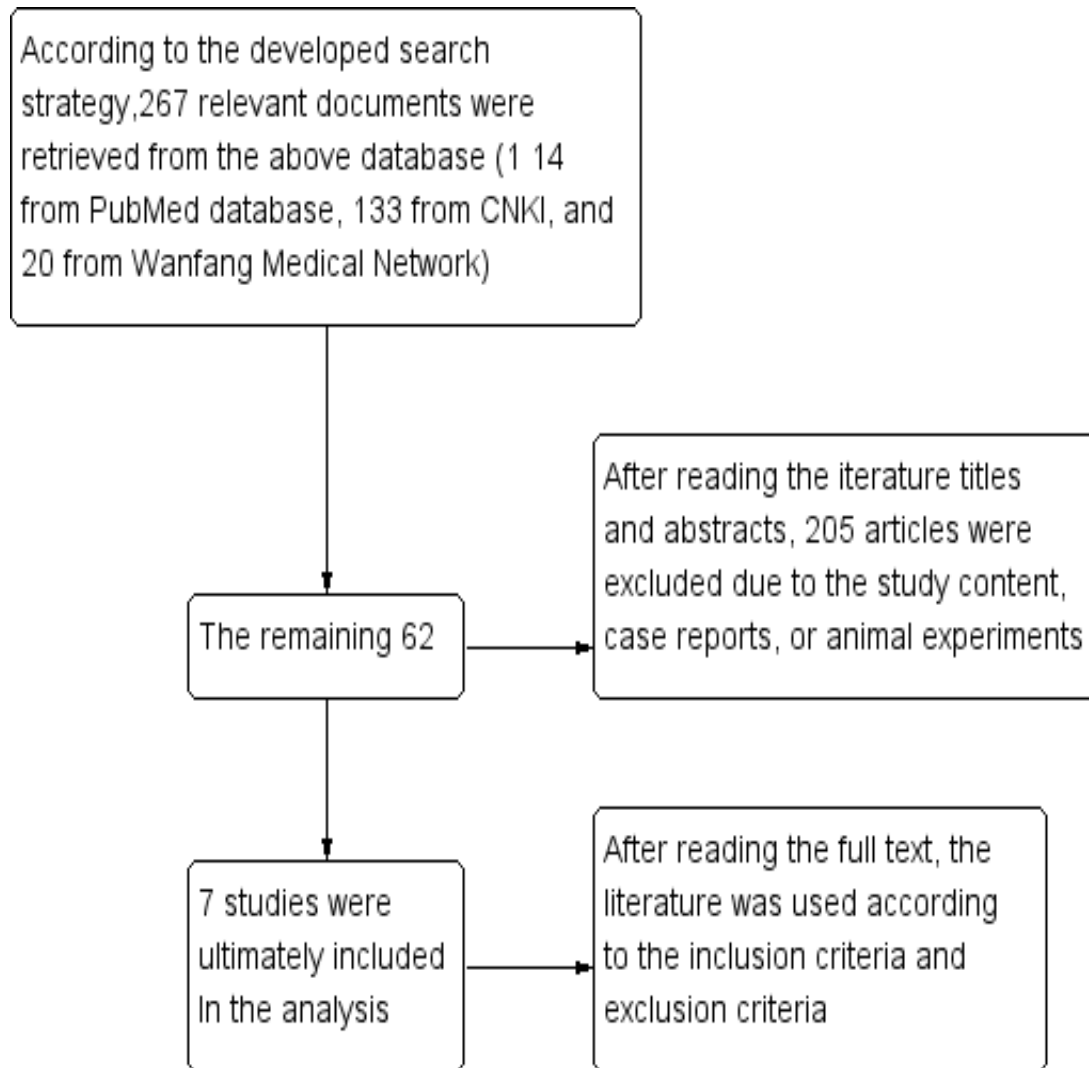


Figure 1: Flow chart for literature search

3.2 Basic Characteristics of the Included Research Literature

A series of 7 publications was included with a total of 516 subjects, of which 216 were in the total number of TP cases, 204 in the total number of TN cases, 43 in the total number of FP cases and 53 in the total number of FN cases. 1 literature was diagnosed with T2WI as a control, and the same pathological and diagnostic findings were used as the gold standard in the remaining 6 publications; 5 were prospective studies and 2 were retrospective studies. The basic information on the characteristics of the literature is as detailed in Tab 1.

Table 1: Basic characteristics of the included literature

AUTHOR	COUNTRY	YEAR OF PUBLICATION	TOTAL NUMBER OF SUBJECTS	CROSS-REFERENCING DIAGNOSTIC MODALITIES (OR THE 'GOLD STANDARD' OF DIAGNOSIS)	TYPE OF STUDY	TP	TN	FP	FN
(Z. Zhang, Du, & Chen, 2022)	China	2022	100	Pathological diagnosis	Forward-looking	46	44	6	4
(L. Wang, Lan, & Zhang, 2017)	China	2017	100	Pathological biopsy	Retrospective	31	45	5	19
(X. Zhang, Quan, & Lu, 2014)	China	2014	75	T ₂ WI	Forward-looking	40	24	7	4
(Shan & Ma, 2020)	China	2020	37	Pathological diagnosis	Forward-looking	20	8	4	5
(Pan, Zhang, & Li, 2012)	China	2012	62	Pathological diagnosis	Retrospective	22	24	3	13
(Zhu & Tai, 2021)	China	2021	70	Pathological diagnosis	Forward-looking	28	29	9	4
(Rao, 2021)	China	2021	72	Pathological diagnosis	Forward-looking	29	30	9	4

3.3 Evaluation of the Quality of the Included Literature

All of the included seven papers made reference to random allocation, five of the prospective studies and two of the retrospective studies, all of which did not describe the allocation of concealment, the blind selectivity and any other sources of bias.

The results of the Cochrane risk of bias assessment in RevMan 5.3 showed that most included studies had high quality, but some were biased in the case selection profile, the number of trials to be evaluated and the setting of the gold standard. The results of the quality assessment of the Cochrane Risk of Bias Assessment tool are detailed in Fig 2.

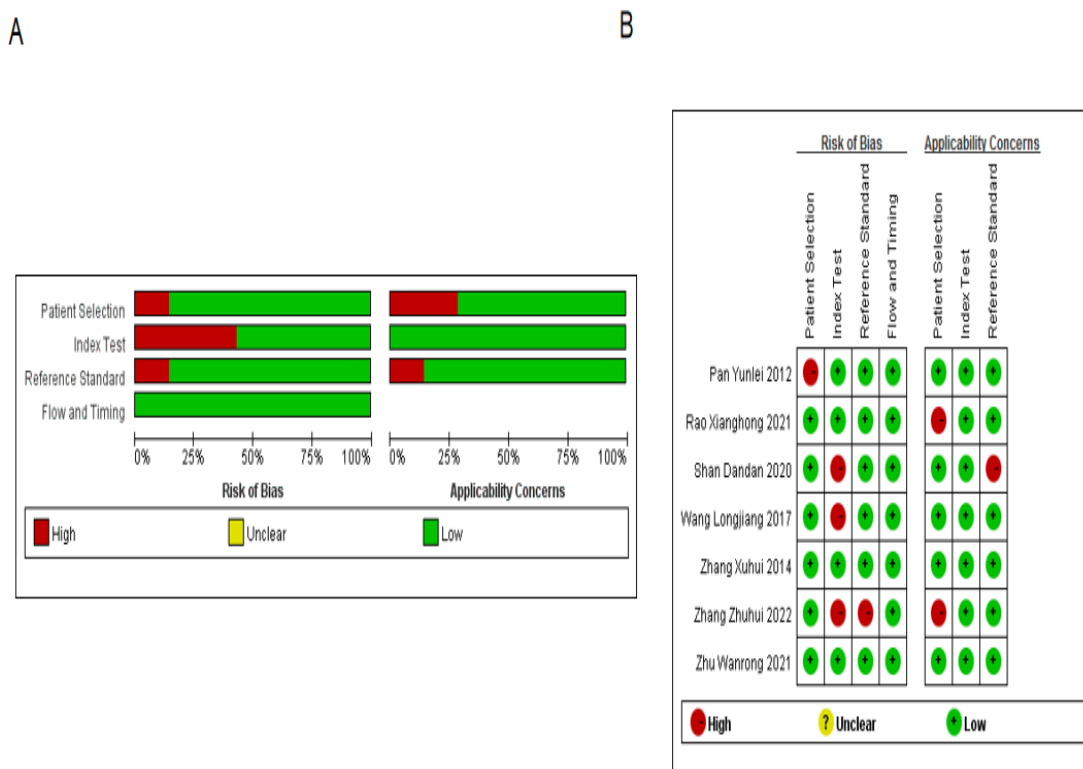


Figure 2: Literature quality evaluation chart

(A. Quality evaluation bar chart; B. Risk offset entries and applicability summary chart.)

3.4 Meta-Analysis of Diagnostic Results

The meta-analysis of the 3.0 T MR dynamic enhancement for the diagnostic test of the prostate cancer showed a combined sensitivity as well as its 95% CI of 0.82 (0.73, 0.90), a combined specificity as well as its 95% CI of 0.83 (0.77, 0.88), a combined positive likelihood ratio as well as its 95% CI of 4.91 (3.25, 7.16), a combined negative likelihood ratio as well as its 95% CI was 0.21 (0.12, 0.26), the combined diagnostic advantage ratio and its 95% CI was 35.28 (16.57, 40.32), and the AUC and its 95% CI was 0.86 (0.81, 0.92). The details are shown in Fig 3, 4 and 5.

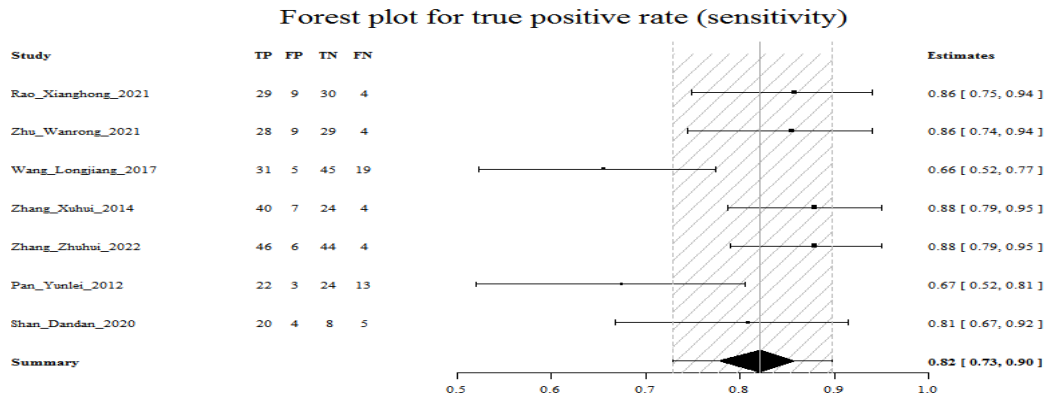


Figure 3: Merged sensitivity forest diagram

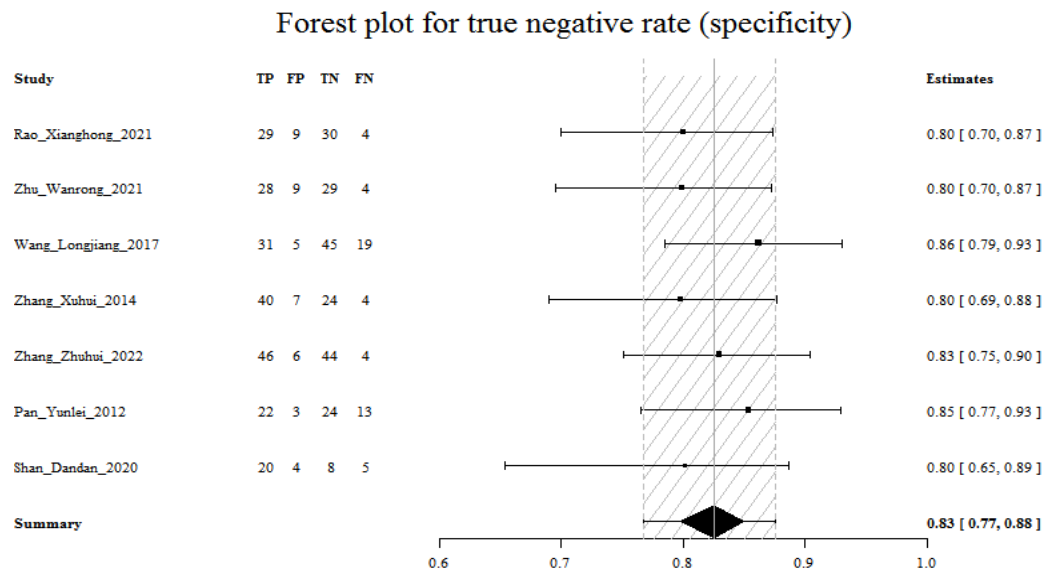


Figure 4: Merged specificity forest plot

SROC Plot

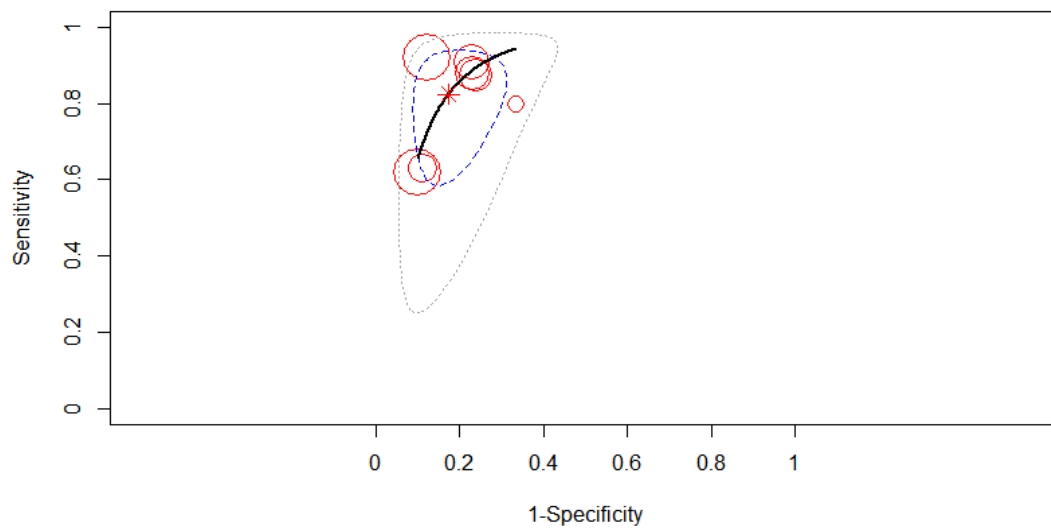


Figure 5: SROC graph

3.5 Heterogeneity Test

This study used correlation from the log of sensitivity to that of (1-specificity) to evaluate for threshold effect-induced the heterogeneity. The results showed that there was no the threshold of effect induced by heterogeneity ($I^2=27.3\%$, $P>0.01$) that the SROC curve showed that the scatter did not have a shoulder and arm distribution, see Fig 5. the Cochran's Q test and I^2 were used to be used to evaluate the non-threshold of effect induced of heterogeneity. The results of this test suggested that both the specificity combined with the sensitivity combined were not subject to any heterogeneity due to non-threshold and were combined when using the fixed effects model.

3.6 Publication Bias

This study was used to assess for publication bias in to the literature using a funnel plot, which revealed that the funnel plot for this study was largely symmetrical ($p=0.412$), which indicates that there is no significant publication bias in this study. This is shown in Fig 6.

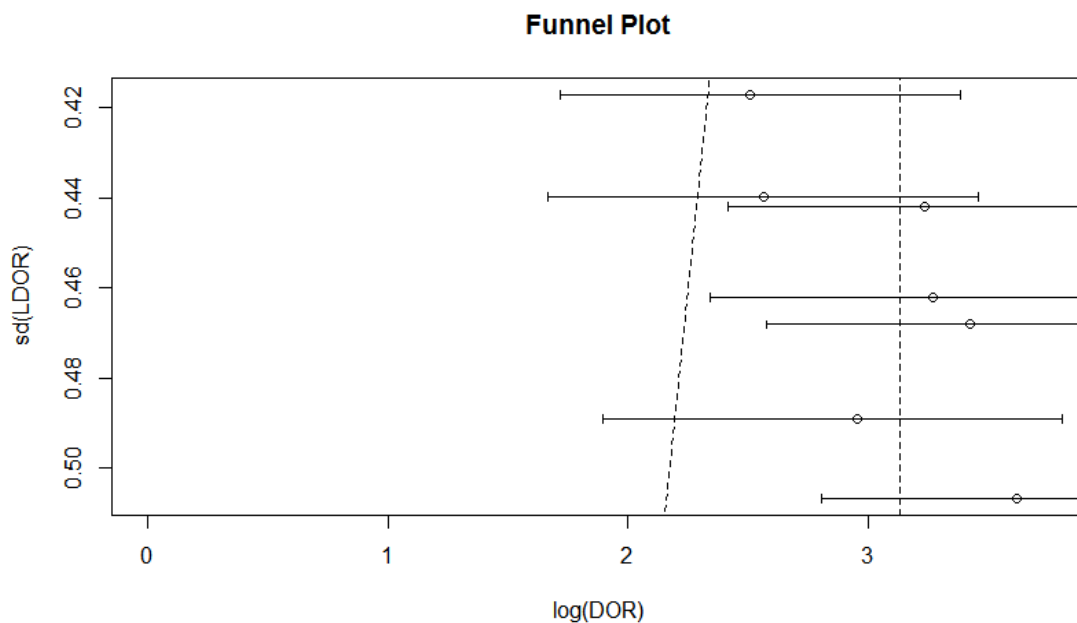


Figure 6: Funnel diagram

4. Discussion

Prostate cancer is a more common malignancy. Early stage of the disease can be completely cured by the use of radical surgery or a radiation therapy, but the more insidious onset of the disease and the lack of obvious early symptoms have resulted in that most patients have been diagnosed at an advanced state of progression or have developed a metastatic tumour, which can seriously affect the outcome of the patient's treatment (MacKay et al., 2021). At the very same time, after radical treatment, biological and chemical

recurrence of that disease often occurs and, to any extent, leads to its progression, which is why an early and more accurate evaluation of the patient's condition is so very important.

At present, the main clinical tool for the diagnosis of this disease is magnetic resonance imaging (MRI) (Bäuerle & Roemer, 2021). MRI has the advantages of a high resolution, multi-parameter, multi-directional and multi-functional imaging. The anatomy of the prostate and the surrounding tissues can be made clearly visible by conventional MRI using T2WI. But research in the clinic has shown that there are some shortcomings in the diagnosis of the conventional MRI for prostate diseases, and it is necessary to use the combination of other examinations to correctly identify between the benign and malignant prostate (Choi, 2021). Dynamic enhanced magnetic resonance imaging is a non-invasive imaging technique used to assess of the physiological characteristics of the tumour and its vasculature. It can determine the formation, dynamics, and the permeability of the blood vessels in the tumour by looking at the concentration of the vessels, the contrast in the tissues, on the basis of the alteration of the tumour angiogenesis and the permeability of the new blood vessels. DCE-MRI shows that the main features of the tumour are increased in blood perfusion of the blood and the density of the blood vessels, which is typical sign of a number of cancers, which includes prostate cancer. Some studies have demonstrated higher microvascular density in prostate cancer tissue, and also an increased microvascular density is more common in the high-grade intraepithelial neoplasia of the prostate and benign prostatic hyperplasia, with there being some overlap between benign prostatic hyperplasia and in prostate cancer (Van Den Berghe, Verstraete, Lecouvet, Lejoly, & Dutoit, 2022). At the same time, it has been well documented that there is a correlation between the microvascular density and the pathological staging, which may be an important indicator for the evaluation of prognosis and a patient's survival. While 3.0T dynamic enhanced magnetic resonance imaging technology can monitor the blood flow by observing the changes in the contrast concentration in tissues and blood vessels, thus improving the accuracy of prostate cancer diagnosis.

The pathological basis of prostate cancer is the rapid proliferation of cancer cells in place of normal tissue. Because of the tight arrangement of cancer cells, the extracellular space becomes smaller, therefore, the blood infiltration in the area of cancer cells is obviously restricted (Winkel, Breit, Block, Boll, & Heye, 2020). The DCE technique can visualize the blood perfusion in the tumor tissue, because the tumor cells have abundant neovascularization and high infiltration rate, so they can enter the tumor tissue rapidly and in large quantities, showing The "fast-in, fast-out" feature. The current study included seven studies on the diagnostic value of 3.0T MR dynamic enhancement for the diagnosis of a prostate cancer (Alexandre, Ricardo, Daniel, Dumitriu, & Salvador, 2018; ALSHAWY, Ibrahim, Hussein, & Lahlah, 2019). The results of

the current study showed that the combined sensitivity of 3.0T MR dynamic enhancement for the diagnosis of the prostate cancer and its 95% CI was 0.82 (0.73, 0.90), the combined specificity and its 95% CI was 0.83 (0.77, 0.88), the combined positive likelihood ratio and its 95% CI was 4.91 (3.25, 7.16), the combined negative likelihood ratio and its 95% CI was 0.21 (0.12, 0.26), and the combined diagnostic advantage ratio and its 95% CI was 35.28 (16.57, 40.32). This is an indication that 3.0T MR with dynamic enhancement has a superior diagnostic effect on the diagnosis of the prostate cancer. The AUC is a measure of the accuracy of a diagnostic of a certain diagnostic method, and the closer the AUC is to 1, the better the diagnosis. The AUC and its 95% CI in this study was 0.86 (0.81, 0.92), indicating a high diagnostic accuracy. However, the most significant limitation of DCE for the diagnosis of prostate cancer is the absence of a method for the assessment of tissue perfusion (X. Wang, Wen, Zhang, & Ji, 2022). The three most common diagnostic methods are: (i) visualization, which is the most straightforward method of ROI with "fast in and fast out", but this approach is influenced only by the diagnostician's ability to read the film and the interpretation of the image can be biased if the work experience of the diagnostician is variable. (ii) Quantitative analysis, in which tumour biology is assessed based on changes in the microvessel density and vascular permeability of the in vivo tumour tissue, usually employs metrics such as the volume transfer constant (K^{trans}), the extracellular extravascular volume fraction (V_e) and the rate constant (k_{ep}), but complex and time-consuming post-processing is used to obtain these quantitative parameters. (iii) Semi-quantitative analysis, in this method, semi-quantitative time signal intensity profiles are being used in order to improve the objective of the diagnosis of dynamic enhancement scans, which include the time of the onset of enhancement, the average and the initial rising gradient of the enhancement curve, as well as the peak of the signal intensity (Yang et al., 2023). In the present study, a meta-analysis of the 7 included papers revealed that there is no heterogeneity in the combined specificity and the combined sensitivity results due to non-threshold effects, which may be related to the unification of both diagnostic modalities and criteria. The research on the most appropriate diagnostic modality for 3.0T MR dynamic enhancement is still in the exploratory stage, but its diagnostic value in the clinical setting is unquestionable. Limitations of this study: the literature for this included study was small ($n = 7$); all included were from China and no relevant studies from other countries were included; the independent diagnostic value of 3.0T MR dynamic enhancement for prostate cancer was investigated and no comparison between diagnostic modalities was made; the jets were prostate cancer, not refined tumor lesions.

5. Conclusion:

The meta-analysis underscores the substantial diagnostic efficacy of 3.0T MR Dynamic enhancement in identifying prostate cancer specifically in fitness and athletic populations. The findings exhibit high sensitivity and

specificity, suggesting that this diagnostic method can be particularly valuable for early detection of prostate cancer in individuals with active lifestyles. This highlights the potential for tailored diagnostic approaches in specialized populations, reinforcing the need for considering patient-specific factors in medical imaging and diagnostics. The consistency and reliability of these results, demonstrated by the absence of significant heterogeneity and publication bias, affirm the utility of 3.0T MR Dynamic enhancement as a robust diagnostic tool in the context of prostate cancer among physically active and athletic individuals.

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