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18F-FDG PET/MR for diagnosis of primary central nervous system lymphoma: protocol for a systematic review and meta-analysis

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ABSTRACT

Background Primary central nervous system lymphoma (PCNSL) is a rare form of extranodal non-Hodgkin's lymphoma with poor prognosis. 18F-flourodeoxyglucose positron emission tomography (PET)/magnetic resonance (MR) combines the advantages of PET and MR. The aim of this study is to evaluate the validity of PET/MR for the diagnosis of PCNSL by means of a meta-analysis.

Methods and analysis Wanfang Database, SinoMed, China National Knowledge Infrastructure, the Cochrane Library, PubMed and Embase will be searched for candidate studies about PET/MRI in PCNSL diagnosis from database inception to October 2024. The following keywords will be applied: "Primary central nervous system lymphoma", "Primary intracerebral lymphoma", "Positron Emission Tomography Magnetic Resonance" and "PET-MR". Studies meeting the inclusion criteria will be included. Studies without full true positive, false positive, false negative and true negative values; studies reported in languages other than English and Chinese; conference abstracts not available in full text and case reports will be excluded. Quality Assessment of Diagnostic Accuracy Studies will be used to evaluate the study quality. The STATA software (V.15.0) and Meta-Disc software (V.1.4) will be used to carry out meta-analysis. When heterogeneity is evident, subgroup analysis will be used to investigate the origin of heterogeneity. The robustness of the analysis will be checked with sensitivity analysis.

Ethics and dissemination This research is based on public databases and does not require ethical approval. The results will seek publication in a peer-reviewed journal after the completion of this systematic review and meta-analysis.

PROSPERO registration number CRD42023472570.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ We reported this protocol in compliance with the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols guidelines and prospectively registered on the PROSPERO platform.
⇒ This systematic review and meta-analysis includes both Chinese and English literature.
⇒ Minimal study bias and more standardised data reporting are permitted through rigorous methodology and robust analysis.
⇒ Significant heterogeneity may exist between studies, leading to unstable results.

INTRODUCTION

Primary central nervous system lymphoma (PCNSL) is a rare form of extranodal non-Hodgkin's lymphoma that is highly aggressive, often involving the brain, eyes, spinal cord and leptomeninges, without evidence of systemic lymphoma.[1] PCNSL accounts for approximately 3–4% of all intracranial malignancies and 4–6% of extranodal lymphomas.[2] The prognosis for PCNSL is very poor compared with Hodgkin's lymphoma, with an overall survival of only 1.5 months if left untreated.[3] Early and rapid diagnosis of PCNSL is very important, but obtaining a rapid clinical diagnosis remains challenging because most lesions are located intracranially and do not have a specific clinical presentation.[4] Stereotactic brain biopsy is the gold standard for the diagnosis of PCNSL.[5] However, this operation is risky and does not apply to all patients.[6] Imaging is the key to PCNSL and can play a crucial role in the non-invasive diagnosis of PCNSL.

Enhanced MRI is the first line of recommended imaging for suspected intracranial tumours including PCNSL.[7] Although MRI features are suggestive of PCNSL, they cannot clearly distinguish PCNSL from other lesions with morphologically similar diseases, such as infectious diseases, metastases and glioblastomas.[8] In modern oncology diagnosis, 18F-flourodeoxyglucose positron emission tomography (18F-FDG PET) with or without CT scan is the most commonly used functional imaging modality.[9] PET with or without CT is also used in the diagnosis of PCNSL.[10] A recent meta-analysis that included 29 original studies suggested the acceptably high diagnostic accuracy of pretreatment FDG-PET(CT) scan in patients with PCNSL.[7]

18F-FDG PET/magnetic resonance (18F-FDG PET/MR) combines the advantages of high sensitivity and bioinformatic visualisation of PET and high resolution and feature parameter diversification of MRI.[11] PET/MR has advantages in the detection of muscle and soft tissue, parenchymal organs, and central neurological lesions and reduction of radiation dose.[12] PET/MR is also recommended for the diagnosis of PCNSL and has shown good agreement with PET/CT in the diagnosis of PCNSL in some studies.[13 14] However, the diagnostic efficacy of PET/MR in diagnosing PCNSL is still unknown, and there is no relevant systematic review and meta-analysis to provide evidence-based medical evidence for this topic. Therefore, the aim of this study is to evaluate the validity of PET/MR for the diagnosis of PCNSL by means of a meta-analysis.

METHODS

Design and registration

We will conduct a systematic review and meta-analysis of PET/MR for the diagnosis of PCNSL. This study will be reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis for Diagnostic Test Accuracy guideline.[15] The study protocol was completed in compliance with the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols guidelines and registered on the PROSPERO platform with the number of CRD42023472570.[16]

Information sources

Electronic databases that include Wanfang Database, SinoMed, China National Knowledge Infrastructure, the Cochrane Library, PubMed and Embase will be searched for relevant candidate articles from database inception to October 2024. We will conduct an updated search before the study is completed. We will further evaluate additional candidate articles by hand searching references in the review or meta-analysis.

Search strategy

Effective search strategies for each database will be designed by XQ and HZ. We will not impose any language or time limits in the implementation of the search process. Search strategy of PubMed is presented as follows:

#1 "Primary central nervous system lymphoma" OR "Primary CNS lymphoma" OR "Primary intracerebral lymphoma" OR "Primary intracranial lymphoma" OR "Primary spinal cord lymphoma" OR "Primary spinal lymphoma"

#2 "Positron Emission Tomography Magnetic Resonance" OR "MR Scan, PET" OR "PET-MR" OR "PET Scan, MR" OR "PET-MRI"

#3 #1 AND #2

Similar search strategies will be used for other electronic databases (online supplemental file 1).

Eligibility criteria

Type of studies

This study does not impose any restrictions on the study design; studies that evaluate the diagnostic performance of PET/MR for PCNSL may be included, whether they are retrospective or case–control studies.

Participants

Participants with untreated PCNSL, regardless of age, gender or ethnicity.

Index tests

PET/MR will be the index test.

Comparator test

Comparator tests (not the reference standard) are not mandatory, and single-arm studies could be included.

Outcomes

The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), diagnostic OR (DOR) and the areas under summary receiver operating characteristic curves (AUCs) will be considered as the main outcomes.

Reference standard

The pathological diagnosis will be considered as a reference standard.

Target conditions

Full text-accessible original researches will be included. The original study used the reference standard applied in this study protocol. True positive (TP), false positive (FP), false negative (FN) and true negative (TN) values will be reported directly in the included original studies or will be available by calculating. Studies without full TP, FP, FN and TN values; studies reported in languages other than English and Chinese; conference abstracts not available in full text and case reports will be excluded.

Literature screening and selection

We will import the articles searched from each electronic database into EndNote (V.9.2) for literature management. We will conduct literature screening based on the inclusion and exclusion criteria identified in this study protocol. Two investigators (XQ and HZ) will screen the literature independently; if there is a dispute upon cross-checking, the decision will be discussed with a third investigator (BS). The two investigators will confirm whether the study meets the inclusion criteria by reading the title, abstract and then the full text.

Data extraction

We will extract relevant data from each included study. Study characteristics and PET/MR correlation results will be the main extracted data. The study characteristics included these factors: the first author's name; publication year; country; study design; number of patients, method of patient selection (such as random and consecutive); type of lesion; type of sample (such as brain tissue or stereotactic biopsy specimen). PET/MR correlation results included TP, FP, FN and TN values, and maximum standardised uptake value. The same two investigators as in the literature screening process will perform the

data extraction independently, and any disputes will be resolved using the same methodology as in the literature screening phase.

Methodological quality assessment

Quality Assessment of Diagnostic Accuracy Studies will be used to assess the methodological quality of each individually included study.[17] This revised assessment tool includes four domains (patient selection, index test, reference standard, and flow and timing). The same two investigators will evaluate the risk of bias and applicability for each included study independently. Disputes will be resolved through discussion with a third investigator. Egger's test and funnel plots will be used to carry out a formal assessment of publication bias.[15]

Data synthesis and statistical analysis

TP, FP, FN and TN values extracted from each individually included study will be used to estimate the pooled sensitivity, specificity, PPV, NPV, DOR and their 95% CI. We will use I^2 statistics to assess heterogeneity between studies. An I^2 of 0% will indicate no heterogeneity between studies, and an I^2 greater than 50% will indicate significant heterogeneity between studies. When significant heterogeneity is indicated, we will explore the sources of heterogeneity through subgroup analysis and meta-regression analysis. Subgroup analysis and meta-regression analysis will be performed on predefined parameters, as we determined during the data extraction phase, such as different study design, method of patient selection, type of lesion and type of sample. The robustness of analyses will be checked by sensitivity analyses. AUC with 95% CI will be subsequently calculated. Threshold effect will be assessed using Spearman's correlation between sensitivity and specificity. Stata V.15.0 (Stata Corp, College Station, Texas, USA) with the *midas* command[18] and Meta-Disc software (V.1.4, Clinical Biostatistics Ramón y Cajal Hospital, Madrid, Spain) will be used to perform meta-analysis. A p value less than 0.05 will be considered statistically significant for the analysis.

Evidence evaluation

The Grading of Recommendations Assessment, Development and Evaluation guideline will be used to evaluate the quality of evidence.[19] According to this guideline, the quality of evidence will be classified into four levels: high, moderate, low and very low. Factors (such as study design, patient populations, outcomes, risk of bias) that can determine and decrease the quality of the evidence will be evaluated to confirm the level of evidence.[19]

Patient and public involvement

None.

ETHICS AND DISSEMINATION

This research is based on public databases and does not require ethical approval. The results will seek publication in a peer-reviewed journal after the completion of this systematic review and meta-analysis.

Contributors XQ, HZ and BS conceived of the study and initiated the study design. XQ and HZ designed search strategies. XQ and HZ wrote the original draft. XQ and BS reviewed and edited the draft. FZ provided supervision. All authors contributed to the refinement of the study protocol.

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Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not applicable.

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