INPLASY PROTOCOL

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None declared.

Effectiveness of magnetic resonance imaging for the diagnosis of central nervous system tuberculosis: A protocol of systematic review and meta-analysis

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Review question / Objective: **Central nervous system tuberculosis (CNSTB) is critical and the prognosis is poor. The current early diagnosis of CNSTB is extremely challenging. Magnetic resonance imaging (MRI) has been shown to be useful in the diagnosis of CNSTB. The aim of the study is to conduct a systematic review and meta-analysis to assess the diagnostic efficacy of MRI for CNSTB in order to better understand the role of MRI in the diagnosis of CNSTB.**
Information sources: **Until June 2022, we will search the commonly used Chinese and English databases to identify studies of MRI diagnosis of CNSTB, including SinoMed, Wanfang database, and China National Knowledge Infrastructure (CNKI) in Chinese and Embase, the Cochrane Library, and Pubmed in English. We will conduct an updated search before the study is completed. References from relevant reviews and meta-analyses will also be searched by hand to identify potentially eligible studies.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 14 December 2021 and was last updated on 14 December 2021 (registration number INPLASY2021120066).

INTRODUCTION

Review question / Objective: **Central nervous system tuberculosis (CNSTB) is critical and the prognosis is poor. The current early diagnosis of CNSTB is extremely challenging. Magnetic resonance imaging (MRI) has been shown to be useful in the diagnosis of CNSTB. The aim of the study is to conduct a systematic review and meta-analysis to assess the diagnostic efficacy of MRI for CNSTB in order to better**

understand the role of MRI in the diagnosis of CNSTB.

Condition being studied: Tuberculosis (TB) remains a major global public health challenge. In 2020, 9.87 million new TB cases and about 1.5 million deaths worldwide, with TB as the number one cause of death from a single source of infection. Depending on the site of Mycobacterium tuberculosis (MTB) infection (involved in the lungs or not), TB can be broadly divided into pulmonary TB and extrapulmonary TB (EPTB). The incidence of central nervous system TB (CNSTB) is low, accounting for only 1-5% of new cases, but the disease is critical and the prognosis is poor, with severe disability or death occurring in about half of cases. The main cause of these serious adverse outcomes is the lack of available early and valid diagnostic methods, leading to delays in diagnosis and treatment. CNSTB mainly includes tuberculous meningitis (TBM) and cerebral TB, the most common of which is TBM. The diagnosis of CNSTB usually requires invasive procedures to obtain specimens, the most common being lumbar puncture to obtain cerebrospinal fluid (CSF) specimens. Invasive procedures carry certain risks and require patient cooperation. CSF testing is of greater diagnostic significance for TBM, while its diagnostic significance is limited for cerebral TB that does not invade the meninges. In contrast, the risk of puncture of the brain parenchyma is enormous and is applied less frequently. On the other hand, the MTB content in CSF is low and the sensitivity of the commonly used acid-fast bacilli smear and MTB cultures is still poor and does not meet the need for early, effective diagnosis. Even with the use of CSF for nucleic acid amplification tests to improve the diagnostic efficacy of TBM, the current results are still unsatisfactory. Rapid and effective diagnosis is the cornerstone of accurate treatment, therefore, for CNSTB, a safe and effective rapid diagnostic tool is urgently needed to improve the prognosis. Imaging, especially magnetic resonance imaging (MRI), is the most commonly used test for CNS lesions, which can show the entire CNS lesions. The advantage of MRI is that it is non-invasive and free of radiation hazards. MRI has been shown to be useful in the diagnosis of CNSTB, not only for intracerebral TB, but also for TBM. However, there is no evidence-based medical evidence to evaluate the diagnostic efficacy of MRI for CNSTB. Therefore, we designed this study to conduct a systematic review and meta-analysis to assess the diagnostic efficacy of MRI for CNSTB in order to better understand the role of MRI in the diagnosis of CNSTB.

METHODS

Search strategy: #1 “Intracranial tuberculosis” OR “cerebral tuberculosis” OR “central nervous system tuberculosis” OR “CNS tuberculosis” OR “brain tuberculomas” OR “brain tuberculosis” OR "Tuberculosis, Meningeal"[Mesh] OR “Meningeal Tuberculoses” OR “Meningeal Tuberculosis” OR “Tuberculoses, Meningeal” OR “TB Meningitis” OR “TB Meningitides” OR “Tubercular Meningitis” OR “Meningitides, Tubercular” OR “Meningitis, Tubercular” OR “Tubercular Meningitides” OR “Meningitis, Tuberculous” OR “Meningitides, Tuberculous” OR “Tuberculous Meningitides” OR “Tuberculous Meningitis” OR “Tuberculosis Meningitis” OR “Meningitides, Tuberculosis” OR “Meningitis, Tuberculosis” OR “Tuberculosis Meningitides” OR “Tuberculous Hypertrophic Pachymeningitis” OR “Hypertrophic Pachymeningitides, Tuberculous” OR “Hypertrophic Pachymeningitis, Tuberculous” OR “Pachymeningitides, Tuberculous Hypertrophic” OR “Pachymeningitis, Tuberculous Hypertrophic” OR “Tuberculous Hypertrophic Pachymeningitides” #2 "Magnetic Resonance Imaging"[Mesh] OR “Imaging, Magnetic Resonance” OR “NMR Imaging” OR “Imaging, NMR” OR “Tomography, NMR” OR “Tomography, MR” OR “MR Tomography” OR “NMR Tomography” OR “Steady-State Free Precession MRI” OR “Steady State Free Precession MRI” OR “Zeugmatography”

OR "Imaging, Chemical Shift" OR "Chemical Shift Imagings" OR "Imagings, Chemical Shift" OR "Shift Imaging, Chemical" OR "Shift Imagings, Chemical" OR "Chemical Shift Imaging" OR "Magnetic Resonance Image" OR "Image, Magnetic Resonance" OR "Magnetic Resonance Images" OR "Resonance Image, Magnetic" OR "Magnetization Transfer Contrast Imaging" OR "MRI Scans" OR "MRI Scan" OR "Scan, MRI" OR "Scans, MRI" OR "Tomography, Proton Spin" OR "Proton Spin Tomography" OR "fMRI MRI, Functional" OR "Functional MRI" OR "Functional MRIs" OR "MRIs, Functional" OR "Functional Magnetic Resonance Imaging" OR "Magnetic Resonance Imaging, Functional" OR "Spin Echo Imaging" OR "Echo Imaging, Spin" OR "Echo Imagings, Spin" OR "Imaging, Spin Echo" OR "Imagings, Spin Echo" OR "Spin Echo Imagings" #3 #1 AND #2.

Participant or population: Untreated CNSTB participants, whether children or adults, regardless of race and gender.

Intervention: MRI will be considered as the index test.

Comparator: Comparative tests (not the reference standard) will be not mandatory in this study, as long as studies reporting the diagnostic efficacy of MRI for the diagnosis of CBSTB, whether single-arm or two-arm, will be included.

Study designs to be included: Studies that evaluated the diagnostic efficacy of MRI for the diagnosis of CNSTB will be included, regardless of the type of study.

Eligibility criteria: Original studies that meet the eligibility criteria and report clear reference criteria for compliance with this protocol will be included. In the original study, the true positive (TP), false positive (FP), false negative (FN), and true negative (TN) values for the MRI diagnosis of CNSTB could be extracted directly or obtained by calculation. If sufficient data were not reported in the original studies to obtain these values, we will contact the authors of the original studies to obtain additional information. Studies that cannot extract full TP, FP, FN, TN values, studies published in languages other than English and Chinese, abstracts that do not report the full text, and case reports will be excluded.

Information sources: Until June 2022, we will search the commonly used Chinese and English databases to identify studies of MRI diagnosis of CNSTB, including SinoMed, Wanfang database, and China National Knowledge Infrastructure (CNKI) in Chinese and Embase, the Cochrane Library, and Pubmed in English. We will conduct an updated search before the study is completed. References from relevant reviews and meta-analyses will also be searched by hand to identify potentially eligible studies.

Main outcome(s): The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and the areas under summary receiver operating characteristic (SROC) curves (AUC) of the MRI in diagnosing of CNSTB will be considered as the main outcomes.

Data management: We will use Endnote version 9.2 to manage the original study obtained by searching each database. We will screen the literature based on the criteria for inclusion and exclusion identified in this protocol. Two independent researchers will conduct literature screening by carefully reading the title, abstract and full text to confirm whether the studies meet the criteria for this study. They will be cross-checked to ensure consistency of results, and if there are differences in the results between the two, the final results will be determined by discussion with a third investigator. After identifying the included studies, we will extract relevant information from the included studies, including general characteristics of the studies and information related to the diagnosis of CNSTB using MRI. The general study characteristics include the name of the first author, year of study publication, country where the study is conducted, type of study design, type of patient selection, sample size, type of CNSTB. Relevant data for the

diagnosis of CNSTB using MRI include TP, FP, FN, TN values, type of MRI (enhanced or not), and type of MRI parameters. As in the literature screening phase, two independent researchers will extract relevant data, and inconsistencies will be resolved through discussions with a third investigator.

Quality assessment / Risk of bias analysis: We will use Quality Assessment of Diagnostic Accuracy Studies (QUADAS-2) to evaluate the methodological quality of each included study. This revised assessment tool includes 4 domains (patient selection, index test, reference standard, and flow and timing). The same two independent investigators will conduct the methodological quality evaluation of each included study and cross-check, and disputed areas will be resolved through discussion with a third investigator.

Strategy of data synthesis: The TP, FP, FN, TN values obtained from the original studies for the diagnosis of CNSTB using MRI will be used to calculate the pooled sensitivity, specificity, PPV, NPV and their corresponding 95% confidence intervals (CIs). We will use I2 statistics to assess heterogeneity between included studies. An I2 value equal to 0% indicates no heterogeneity between studies, and an I2 value greater than 50% indicates significant heterogeneity between studies. We will likewise calculate the combined AUC and the corresponding 95% CI. Stata version 15.0 (Stata Corp., College Station, TX, USA) with the midas command [4] and RevMan version 5.3 (Cochrane Collaboration, Oxford, United Kingdom) will be used to perform meta-analysis and generate forest plots and SROC curves. A p-value < 0.05 will be considered statistically significant for the relevant statistical analysis.

Subgroup analysis: When there is significant heterogeneity between studies, we will explore possible sources of heterogeneity through subgroup analysis and meta-regression analysis, if a sufficient number of studies are included. Subgroup analysis and meta-regression analysis will be conducted on different types of study design, types of patient selection, types of CNSTB, types of MRI, and types of MRI parameters.

Sensitivity analysis: We will use sensitivity analysis to evaluate the robustness of the correlation analysis.

Language: No restriction.

Country(ies) involved: China.

Keywords: central nervous system, tuberculosis, accuracy, MRI, sensitivity, meta-analysis.

Contributions of each author:
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Author 2 - Xudong Xu.
Author 3 - Jun Yang.
Author 4 - Hong Zheng.