INPLASY PROTOCOL

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Review Stage at time of this submission: The review has not yet started.

Conflicts of interest: No.

Impact of thyroid ultrasonography combined ultrasound-guided fineneedle aspiration biopsy in detection thyroid microcarcinoma: A protocol of systematic review

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Review question / Objective: Does thyroid ultrasonography (TUS) combined ultrasound-guided fine-needle aspiration biopsy (UGFNAB) accurately detect thyroid microcarcinoma (TMC)?

Condition being studied: Thyroid ultrasonography; ultrasoundguided fine-needle aspiration biopsy; thyroid microcarcinoma. Information sources: Electronic searches - The following resources will be comprehensively searched in PUBMED, EMBASE, Cochrane Library, Web of Science, Scopus, Chinese Biomedical Literature Database, and China National Knowledge Infrastructure from the inception to the June 1, 2020 regardless language and publication status limitations. A draft search strategy for PUBMED is exerted. We will modify similar search strategies for other electronic databases. Other resources - This study will also identify other resources, such as clinical trial registry for ongoing trials, and reference lists of included studies.

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 12 July 2020 and was last updated on 12 July 2020 (registration number INPLASY202070048).

INTRODUCTION

Review question / Objective: Does thyroid ultrasonography (TUS) combined ultrasound-guided fine-needle aspiration biopsy (UGFNAB) accurately detect thyroid microcarcinoma (TMC)? **Condition being studied:** Thyroid ultrasonography; ultrasound-guided fineneedle aspiration biopsy; thyroid microcarcinoma.

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METHODS

Participant or population: Reports of study involved patients with histological-proven TMC will be included in this study, regardless the country, race, age and gender.

Intervention: Index test: any forms of TUS combined UGFNAB will be used to detect patients with TMC.

Comparator: Reference test: participants with histological-proven TMC will be utilized in the control group.

Study designs to be included: We will include all potential case-control studies (CCSs) that examined the accuracy of TUS combined UGFNAB in detection of TMC.

Eligibility criteria: We will include all CCSs that examined the accuracy of TUS combined UGFNAB in detection of TMC. There are not limitations related to the basis of language of publications.

Information sources: Thyroid ultrasonography; ultrasound-guided fineneedle aspiration biopsy; thyroid microcarcinoma.

Information sources: Electronic searches -The following resources will be comprehensively searched in PUBMED, EMBASE, Cochrane Library, Web of Science, Scopus, Chinese Biomedical Literature Database, and China National Knowledge Infrastructure from the inception to the June 1, 2020 regardless language and publication status limitations. A draft search strategy for PUBMED is exerted. We will modify similar search strategies for other electronic databases. Other resources - This study will also identify other resources, such as clinical trial registry for ongoing trials, and reference lists of included studies.

Main outcome(s): The primary outcomes include sensitivity and specificity. The secondary outcomes are positive likelihood ratio, negative likelihood ratio, and diagnostic odds ratio. Data management: Two authors will separately collect data from all included studies by a previous designed data extraction sheet. Any divisions between two authors will be settled by a third author through discussion. The collected information includes study information (e.g. title, first author, time of study, country, study setting, and sample size), study design and methods, patient characteristics (e.g. age, sex, and diagnosis details), details of index and reference tests, outcome indicators, results, and findings.

Quality assessment / Risk of bias analysis: Quality Assessment of Diagnostic Accuracy Studies tool will be utilized to appraise the methodological quality for all included studies. Its total score ranges from 0 to 14, with higher score indicating better study quality. Any differences between two authors will be solved by discussion with a third author invited.

Strategy of data synthesis: This study will apply RevMan V.5.3 and Stata V.12.0 softwares to perform statistical analysis. All outcome data will be estimated as descriptive statistics and 95% confidence intervals. We will use I2 statistic test to investigate the heterogeneity across studies. $I2 \leq 50\%$ suggests homogeneity, and a fixed-effects model will be employed. Otherwise, I2 >50% indicates distinct heterogeneity, and a random-effects model will be placed. We will use collected data to calculate values of sensitivity, specificity, positive likelihood ratio, negative likelihood ratio, and diagnostic odds ratio by 2 x 2 tables. In addition, a descriptive forest plot and a summary receiver operating characteristic plot will be created. Whenever possible, we will carry out a meta-analysis if homogeneity is identified. Otherwise, we will conduct a subgroup analysis to examine the sources of evident heterogeneity. If we can not perform a meta-analysis after subgroup analysis, we will utilize bivariate random-effects regression approach to plot the estimates of sensitivity and specificity.

Subgroup analysis: If necessary, this study will perform a subgroup analysis to identify possible sources of apparent heterogeneity according to the variations in the study and characteristics, study quality and outcome indicators.

Sensibility analysis: If possible, this study will carry out a sensitivity analysis to test the robustness of study results by removing low quality studies.

Country(ies) involved: China.

Keywords: Thyroid microcarcinoma; ultrasound-guided fine-needle aspiration biopsy; thyroid ultrasonography; sensitivity; specificity.

Contributions of each author:

Author 1 - Zhuan-ning Han. Author 2 - Zhe Liu. Author 3 - Jing Wang.