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

Zhuan-Ning Han, MB[a], Zhe Liu, MB[b], Jing Wang, MB[c],*

Abstract

Background: This study aims to explore the accuracy of thyroid ultrasonography (TUS) combined ultrasound-guided fine-needle aspiration biopsy (UGFNAB) for detection of thyroid microcarcinoma (TMC).

Methods: A comprehensive search in PUBMED, EMBASE, Cochrane Library, Web of Science, Scopus, Chinese Biomedical Literature Database, and China National Knowledge Infrastructure from the beginning to the June 1, 2020 without language and publication status limitations. Two authors will independently perform articles identification, data extraction and assessment of study quality. Any disagreements will be resolved by discussion with a third author. We will carry out study quality evaluation using Quality Assessment of Diagnostic Accuracy Studies tool, and will employ statistical analysis using RevMan V.5.3 and Stata V.12.0 softwares.

Results: We will summarize current evidence to investigate the accuracy of TUS combined UGFNAB in detection of TMC.

Conclusion: The findings of this study may provide helpful evidence of TUS combined UGFNAB in detection of TMC.

Study registration: INPLASY202070048.

Abbreviations: CCSs = case-control studies, CIs = confidence intervals, PRISMA = preferred reporting items for systematic reviews and meta-analysis, TC = thyroid carcinoma, TUS = thyroid ultrasonography, UGFNAB = ultrasound-guided fine-needle aspiration biopsy.

Keywords: sensitivity, specificity, thyroid microcarcinoma, thyroid ultrasonography, ultrasound-guided fine-needle aspiration biopsy

1. Introduction

Thyroid carcinoma (TC) is the most common endocrine malignant cancer.[1–4] It comprises of papillary carcinoma, follicular carcinoma, Hürthle cell carcinoma, medullary thyroid carcinoma, and anaplastic carcinoma.[4–6] Of those, papillary TC represents the most common type, and accounts for 80% of all cases.[7,8] Papillary thyroid microcarcinoma (TMC) is defined as less than 10 mm in diameter.[9–11] Its treatments vary according its detection and diagnosis.

Thyroid ultrasonography (TUS) and ultrasound-guided fine-needle aspiration biopsy (UGFNAB) are reported to diagnose TMC.[12–20] However, no systematic review has been conducted to explore the accuracy of TUS combined UGFNAB in detection of TMC. Thus, this study will systematically assess the diagnostic accuracy of TUS combined UGFNAB for TMC detection.

2. Methods

2.1. Objective

This study aims to assess the accuracy of TUS combined UGFNAB in detection of TMC.

2.2. Study registration

This study was registered on INPLASY202070048, and it was reported based on the guideline of Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) Protocol statement.[21]

2.3. Eligibility criteria for study selection
2.3.1. Types of studies.
We will include all potential case-control studies (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.

2.3.2. Types of participants. Reports of study involved patients with histological-proven TMC will be included in this study, regardless the country, race, age, and gender.

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

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

2.3.4. Types of outcome measurements. The primary outcomes include sensitivity and specificity. The secondary outcomes are positive likelihood ratio, negative likelihood ratio, and diagnostic odds ratio.

2.4. Data sources and search strategy

2.4.1. 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 in Table 1. We will modify similar search strategies for other electronic databases.

2.4.2. Other resources. This study will also identify other resources, such as clinical trial registry for ongoing trials, and reference lists of included studies.

2.5. Data collection and analysis

2.5.1. Selection of studies. Two authors will screen the titles/abstracts of all identified citations separately, and all duplicates and irrelevant literatures will be removed. Full-text of potential studies will be obtained and read carefully to further examine if they fulfill all eligibility criteria. If disagreements occur between two authors, a third author will be invited to figure out by discussion. The results of study selection will be presented in a PRISMA flow chart.

2.5.2. Data collection and 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.

2.5.3. Dealing with missing data. If any insufficient or missing information is examined, we will contact primary corresponding authors to request it. We will analyze available data if we cannot obtain that data, and will discuss its affects to the study findings.

2.6. Methodological quality assessment

Quality Assessment of Diagnostic Accuracy Studies tool[22] 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 2 authors will be solved by discussion with a third author invited.

2.7. Statistical analysis

2.7.1. Data synthesis. This study will apply RevMan V.5.3 and Stata V.12.0 softwares to perform statistical analysis. All

Table 1	
Search strategy of PUBMED.	
Number	**Search terms**
1	Thyroid nodules
2	Thyroid cancer
3	Thyroid carcinoma
4	Thyroid tumor
5	Solid lumps
6	Fluid-filled lumps
7	Head and neck tumors
8	Neck masses
9	Micro
10	Or 1–9
11	Ultrasound
12	Ultrasonography
13	Ultrasonic
14	Guide
15	Guided
16	Cytology
17	Biopsy procedure
18	Fine needle aspiration
19	Diagnosis
20	Detection
21	Or 11–20
22	Case-controlled study
23	Case-control study
24	Case study
25	Controlled study
26	Observational study
27	Case-referent study
28	Comparator
29	Control
30	Or 22–29
31	10 and 21 and 30

outcome data will be estimated as descriptive statistics and 95% confidence intervals. We will use I^2 statistic test to investigate the heterogeneity across studies. $I^2 \leq 50\%$ suggests homogeneity, and a fixed-effects model will be employed. Otherwise, $I^2 > 50\%$ 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 × 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 cannot perform a meta-analysis after subgroup analysis, we will utilize bivariate random-effects regression approach to plot the estimates of sensitivity and specificity.

2.7.2. 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.

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

2.7.4. Reporting bias. This study will conduct a funnel plot and Egger regression test to examine reporting bias if over 10 studies are included.[23]

2.8. Ethics and dissemination

This study will not analyze individual patient data, thus, no ethic approval is necessary. Its results will be published at a peer-reviewed journal.

3. Discussion

TMC is a common malignant tumor. Although a variety of diagnosis tool are utilized to detect this disorder, it is still not easy to diagnose at early stage. Previous studies suggested that TUS combined UGFNAB could be used for detection of TMC. However, all results are based on the individual study, and no systematic review specifically investigates the accuracy of TUS combined UGFNAB in detection of TMC. Thus, this systematic review will explore the accuracy of TUS combined UGFNAB in detection of TMC. The results of this study may provide helpful evidence for the clinical diagnosis of TMC.

Author contributions

Conceptualization: Zhuan-Ning Han, Zhe Liu, Jing Wang.
Data curation: Jing Wang.
Formal analysis: Zhuan-Ning Han, Zhe Liu, Jing Wang.
Investigation: Jing Wang.
Methodology: Zhe Liu.
Project administration: Jing Wang.
Resources: Zhuan-Ning Han, Zhe Liu.
Software: Zhuan-Ning Han, Zhe Liu.
Supervision: Jing Wang.
Validation: Zhuan-Ning Han, Jing Wang.
Visualization: Zhuan-Ning Han, Jing Wang.
Writing – original draft: Zhuan-Ning Han, Zhe Liu, Jing Wang.
Writing – review & editing: Zhuan-Ning Han, Zhe Liu, Jing Wang.

References

[1] Chiacchio S, Lorenzoni A, Boni G, et al. Anaplastic thyroid cancer: prevalence, diagnosis and treatment. Minerva Endocrinol 2008;33:341–57.

[2] Abonowara A, Quraishi A, Sapp JL, et al. Prevalence of atrial fibrillation in patients taking TSH suppression therapy for management of thyroid cancer. Clin Invest Med 2012;35:E152–6.

[3] Konturek A, Barczyński M, Stopa M, et al. Trends in prevalence of thyroid cancer over three decades: a retrospective cohort study of 17,526 surgical patients. World J Surg 2016;40:538–44.

[4] Bradley EI, Liechty RD. Modified subtotal thyroidectomy for Graves' disease: a two-institution study. Surgery 1983;94:955–8.

[5] Van Vuuren PA, Balm AJ, Gregor RT, et al. Carcinoma arising in thyroglossal remnants. Clin Otolaryngol Allied Sci 1994;19:509–15.

[6] Chrisoulidou A, Boudina M, Tzemailas A, et al. Histological subtype is the most important determinant of survival in metastatic papillary thyroid cancer. Thyroid Res 2011;4:12.

[7] Davies L, Welch HG. Increasing incidence of thyroid cancer in the United States, 1973-2002. JAMA 2006;295:2164–7.

[8] Cappelli C, Braga M, De Martino E, et al. Outcome of patients surgically treated for various forms of hyperthyroidism with differentiated thyroid cancer: experience at an endocrine center in Italy. Surg Today 2006;36:125–30.

[9] Baudin E, Travagli JP, Ropers J, et al. Microcarcinoma of the thyroid gland: the Gustave-Roussy Institute experience. Cancer 1998;83:553–9.

[10] Noguchi S, Yamashita H, Murakami N, et al. Small carcinomas of the thyroid. A long-term follow-up of 867 patients. Arch Surg 1996;131:187–91.

[11] Hay ID, Grant CS, Taylor WF, et al. Ipsilateral lobectomy versus bilateral lobar resection in papillary thyroid carcinoma: a retrospective analysis of surgical outcome using a novel prognostic scoring system. Surgery 1987;102:1088–95.

[12] Jiang XH, Chen J, Wang MY, et al. Diagnostic value of ultrasonography in the aggressiveness of thyroid micropapillary carcinoma without lymph node metastasis. Chin J Clin Med Imaging 2020;31:320–4.

[13] Yuan GS, Huang L, Li Y. Analysis of the value of ultrasound contrast in the diagnosis of thyroid micropapillary carcinoma. Cancer Progr 2020;18:363–5.

[14] Guo YJ, Zhai H, Xu XM. The diagnostic value of high-frequency ultrasound and contrast-enhanced microthyroid papillary carcinoma and their invasiveness. Chin J Inte Trad Western Med Imaging 2020;18:30–3.

[15] Lian F, Sun YK, Tang SF, et al. The diagnostic value of fine needle aspiration of thyroid nodules combined with ultrasound contrast in the diagnosis of early thyroid microcarcinoma. Chin J Comprehensive Clin Med 2020;1:31–5.

[16] Tang M, Li LS, Cheng LX, et al. Accuracy of ultrasound-guided fine needle aspiration biopsy in diagnosis of thyroid microcarcinoma. Modern Pract Med 2019;31:348–50.

[17] Wang Y. Diagnostic value of conventional ultrasound combined with ultrasound contrast in the diagnosis of thyroid micropapillary carcinoma. Henan J Surg 2018;24:94–5.

[18] Yang YQ. The value of contrast-enhanced ultrasound in the differential diagnosis of benign and malignant thyroid microsolid nodules. J Shantou Uni School Med 2018;31:104–5.

[19] Liu J, Yu XM, Peng JY, et al. Clinical and pathological analysis of 992 cases of fine-needle aspiration biopsy guided by ultrasound. Guangdong Med J 2017;38:588–91.

[20] Zhang TY, Chen DF, Li KZ, et al. The diagnostic value of high-frequency ultrasound and guided fine-needle aspiration cytology for the diagnosis of microthyroid nodules. J Jining Med College 2010;33:406–7.

[21] Shamseer L, Moher D, Clarke M, et al. PRISMA-P Group. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. BMJ 2015;349:g7647.

[22] Whiting PF, Rutjes AW, Westwood ME, et al. QUADAS-2: a revised tool for the quality assessment of diagnostic accuracy studies. Ann Intern Med 2011;155:529–36.

[23] Deeks JJ, Macaskill P, Irwig L. The performance of tests of publication bias and other sample size effects in systematic reviews of diagnostic test accuracy was assessed. J Clin Epidemiol 2005;58:882–93.