Heliyon 10 (2024) e24391

Contents lists available at ScienceDirect

Heliyon

journal homepage: www.cell.com/heliyon

Systematic review and meta-analysis

A meta-analysis of the value of serum TSH concentration in the diagnosis of differentiated thyroid cancer in patients with thyroid nodules☆

Xiao-Yu Fan [a], Wei You [b,*], Yao Chen [c], Chen-Cong Nie [c], Xue-Lian Wang [b], Cheng Lei [d], Juan Song [b], Huai-Li Luo [e]

[a] Department of General Surgery, Zigong Fourth People's Hospital, Zigong 643000, Sichuan Province, China
[b] Emergency Department Intensive Care Unit, Zigong Fourth People's Hospital, Zigong 643000, Sichuan Province, China
[c] Department of Nursing, Zigong Fourth People's Hospital, Zigong 643000, Sichuan Province, China
[d] School of Public Health and Management, Chongqing Medical University, Chongqing 400000, Chongqing, China
[e] Department of Cardiovascular Medicine, Mianyang Central Hospital, Mianyang621000, Sichuan Province, China

ARTICLE INFO

Keywords:
Thyroid cancer,TSH,Meta-analysis
Diagnosis, Sensitivity and specificity

ABSTRACT

Background: In recent years, most studies believe that high TSH level is positively correlated with the incidence of thyroid cancer, but it is still controversial. For this reason, the purpose of this study is to analyze the correlation between preoperative TSH level and thyroid malignant nodules using pathological diagnosis as the gold standard. To evaluate the role of serum TSH in predicting malignancy of thyroid nodules with uncertain cytology.As an important member of the hypothalamus–pituitary–thyroid axis in the endocrine system, TSH plays a crucial role in regulating the growth, differentiation, and function of thyroid cells (Zhang et al., 2023) [1]. Therefore, it has always been considered closely related to TC. Currently, most studies have compared the TSH levels of TC patients and individuals with benign thyroid disease or healthy controls. These findings from various studies indicated that TC patients often demonstrate elevated TSH levels, even when their TSH falls within the normal range. However, it is important to highlight that the current evidence primarily relies on cross-sectional studies, which mainly describe a phenomenon without establishing causal relationships. The involvement of TSH in the early onset or late progression of TC remains unknown, the interaction between TSH and other factors and how it affects TC is not well understood (Gubbi et al., 2020) [2].Symptoms of thyroid cancer are usually insidious, and early thyroid cancer often has no obvious clinical symptoms. Therefore, early detection and early treatment are particularly important, and how to improve the preoperative diagnosis rate of thyroid nodules is also a problem that clinicians pay close attention to.

Objective: To evaluate the value of serum TSH concentration in the diagnosis of differentiated thyroid carcinoma in patients with thyroid nodules.

Methods: Our study searched databases in both Chinese and English.China Academic Journals FULL-text Database (CNKI), China Online Journals, Chinese Scientific Journals database and Chinese Biomedical Literature Database (CBM) were searched by computer. The English literature was established by PubMed, Embase, Cochrane Library, Web of Science and other databases until

☆ (This study has been registered on the PROSPERO website (No. CRD42023390168).

* Corresponding author. Department of Emergency Intensive Care Unit, Zigong Fourth People's Hospital, No. 2 Tanmulin Street, Ziliujing District, Zigong 643000, Sichuan Province, China.
E-mail address: 345833016@qq.com (W. You).

https://doi.org/10.1016/j.heliyon.2024.e24391
Received 25 April 2023; Received in revised form 14 December 2023; Accepted 8 January 2024
Available online 17 January 2024

June 2022 to search for relevant literatures on the diagnostic test of serum TSH concentration in patients with thyroid nodule. The literatures that met the criteria were screened, the data were extracted, and the literature quality was evaluated. The sensitivity, specificity, positive likelihood ratio, negative likelihood ratio and diagnostic odds ratio of the method for the diagnosis of differentiated thyroid carcinoma were calculated and summarized. The receiver operating characteristic (SROC) curve was drawn and the area under the curve was obtained.
Results: A total of 23 diagnostic tests were included (5348 lesions). Meta-analysis showed that the combined sensitivity, specificity, positive likelihood ratio, negative likelihood ratio and diagnostic odds ratio of serum TSH concentration in the diagnosis of differentiated thyroid carcinoma were 0.64, 0.72, 2.511, 0.386 and 7.14, respectively. The area under SROC curve (AUC) was 0.79, and the Q index was 0.7283, indicating no statistically significant difference.
Conclusion: Based on current evidence, detection of serum TSH concentration in thyroid nodule patients has high sensitivity and specificity for the diagnosis of differentiated thyroid cancer, which has good clinical application value. However, other auxiliary examinations are still needed to improve the diagnosis rate.

1. Introduction

Thyroid Nodules (TN) is a common Thyroid disease in the world. In the past two decades, with the widespread application of imaging technology including ultrasound, the detection rate of Thyroid Nodules has increased exponentially [1], and the detection rate of Thyroid Nodules in healthy people has been as high as 68 %. Among them, asymptomatic thyroid nodules are about 20%–76 % [2]. Symptoms of thyroid cancer are usually insidious, and early thyroid cancer often has no obvious clinical symptoms. Therefore, early detection and early treatment are particularly important, and how to improve the preoperative diagnosis rate of thyroid nodules is also a problem that clinicians pay close attention to. Horvath et al. drew on breast Imaging Reporting and datasystem (BI-RADS), In 2009, the Thyroid Imaging Reporting and Data System (TI-RADS) was first proposed [3]. After ti-RADS classification was first proposed, thyroid ultrasound reporting was more standardized and the diagnostic accuracy of two-dimensional ultrasound was significantly improved. Later, other more specific classification criteria have been proposed at home and abroad [4,5]. Among them, the ti-rads classification criteria customized by Kwak [6] in 2011 is more suitable for clinical use and similar to bi-rads classification. According to this classification, the five ultrasonic characteristics of nodular solid, hypoechoic, unclear boundary, microcalcification and aspect ratio (A/T) $\geq$1 are considered as suspicious signs of thyroid malignant nodules. According to this classification standard, the preoperative diagnosis of thyroid malignant nodules is greatly improved, but the malignant probability span of Ti-RADS type 4 nodules is very large, ranging from 5 % to 85 % [7]**.** Ti-rads classification can improve the accuracy of preoperative ultrasound diagnosis, but there is a certain misdiagnosis rate for type 4 thyroid nodules. Therefore, how to improve the diagnosis of Ti-RADS type 4 thyroid nodules is also a problem faced by sonographers at present. International guidelines specify which nodules should be examined by fine needle aspiration cytology (FNA) [2,8,9].FNA is clinically safe, cost-effective, minimally invasive, and has few complications [10]. For nodule reports showing cytological uncertainty (TIR3), limitations arise because malignancy cannot be ruled out even if the incidence is relatively low. In this case, molecular testing can represent an opportunity to identify thyroid cancer, although it does not guarantee a correct diagnosis and is relatively costly [11]. Thyroid stimulating hormone (TSH) is a disubunit glycoprotein released by pituitary gland in response to the release of hypothalamic thyrotropin-releasing hormone (TRH). TSH acts on thyroid cell signal transduction through thyrotropin receptor and is responsible for regulating thyroid blood supply and cell proliferation. Recently, serum thyroid stimulating hormone (TSH) levels have been evaluated as predictors of malignancy of thyroid nodules, Elevated serum TSH levels were shown to be associated with an increased risk of thyroid cancer [12] (a simple and free adjuvant cost test for stratifying the risk of malignancy associated with thyroid nodules has not previously been evaluated in thyroid nodules with definitive cytology). Studies have shown that even if TSH is within the normal concentration range, the higher the TSH concentration, the higher the risk of thyroid cancer [13]. Expert consensus on the clinical application of thyroid serum markers also clearly suggests that TSH level is of reference significance in differentiating benign and malignant thyroid nodules to some extent, and routine preoperative use is recommended [14]. Relevant studies have shown [15] that TSH not only promotes thyroid cancer, but also promotes breast cancer, pancreatic cancer, ovarian cancer and other malignant tumors. Although most studies in recent years believe that high TSH level is positively correlated with the incidence of thyroid cancer, there is still controversy. Sohn S et al. [16]. believe that serum TSH has no value in the evaluation of thyroid papillary microcarcinoma. For this reason, the aim of this study was to analyze the correlation between preoperative TSH levels and malignant thyroid nodules using pathological diagnosis as the gold standard to evaluate the role of serum TSH in predicting malignant thyroid nodules with uncertain cytology.

2. Methods

2.1. Literature search

The retrieval strategy follows the PICOS principle (P: Participant; I: Intervention; C) Comparison O: Outcome; S: Study Design developed search strategies for foreign language databases (including PubMed, Web of Science, Cochrane Library, EMbase) and Chinese databases by computer. Including China Biomedical literature Database (CBM), Wanfang Data Medical journal database, VIP

database and CNKI, etc. The retrieval time is from database construction to June 2022.

2.2. Retrieval strategy

The search terms in Chinese database were: (thyroid hormone OR TSH) And (thyroid nodule OR thyroid tumor OR thyroid cancer) And (diagnosis). English Database Search terms: (Thyroid Neoplasms OR Neoplasm, Thyroid OR Thyroid Neoplasm OR Neoplasms, Thyroid OR Thyroid Carcinoma OR Carcinoma, Thyroid OR Carcinomas, Thyroid OR Thyroid Carcinomas OR Cancer of Thyroid OR Thyroid Cancers OR Thyroid Cancer OR Cancer, Thyroid OR Cancers, Thyroid OR Cancer of the Thyroid OR Thyroid Adenoma OR Adenoma, Thyroid OR Adenomas, Thyroid OR Thyroid Adenomas And Thyroid Hormones OR Hormones, Thyroid OR Thyroid Hormone OR Hormone, Thyroid OR TSH And sensitiv*[Title/Abstract] OR sensitivity and specificity [MeSHTerms]OR (predictive [Title/Abstract] AND value*[Title/Abstract]) OR predictive value of tests [MeSH Terms] OR accuracy*[Title/Abstract].

2.3. Inclusion criteria

Inclusion criteria ① Subjects: Thyroid nodule was detected by cervical ultrasound; Thyroid function test was performed on all patients. ② Postoperative pathological results were regarded as the "gold standard".

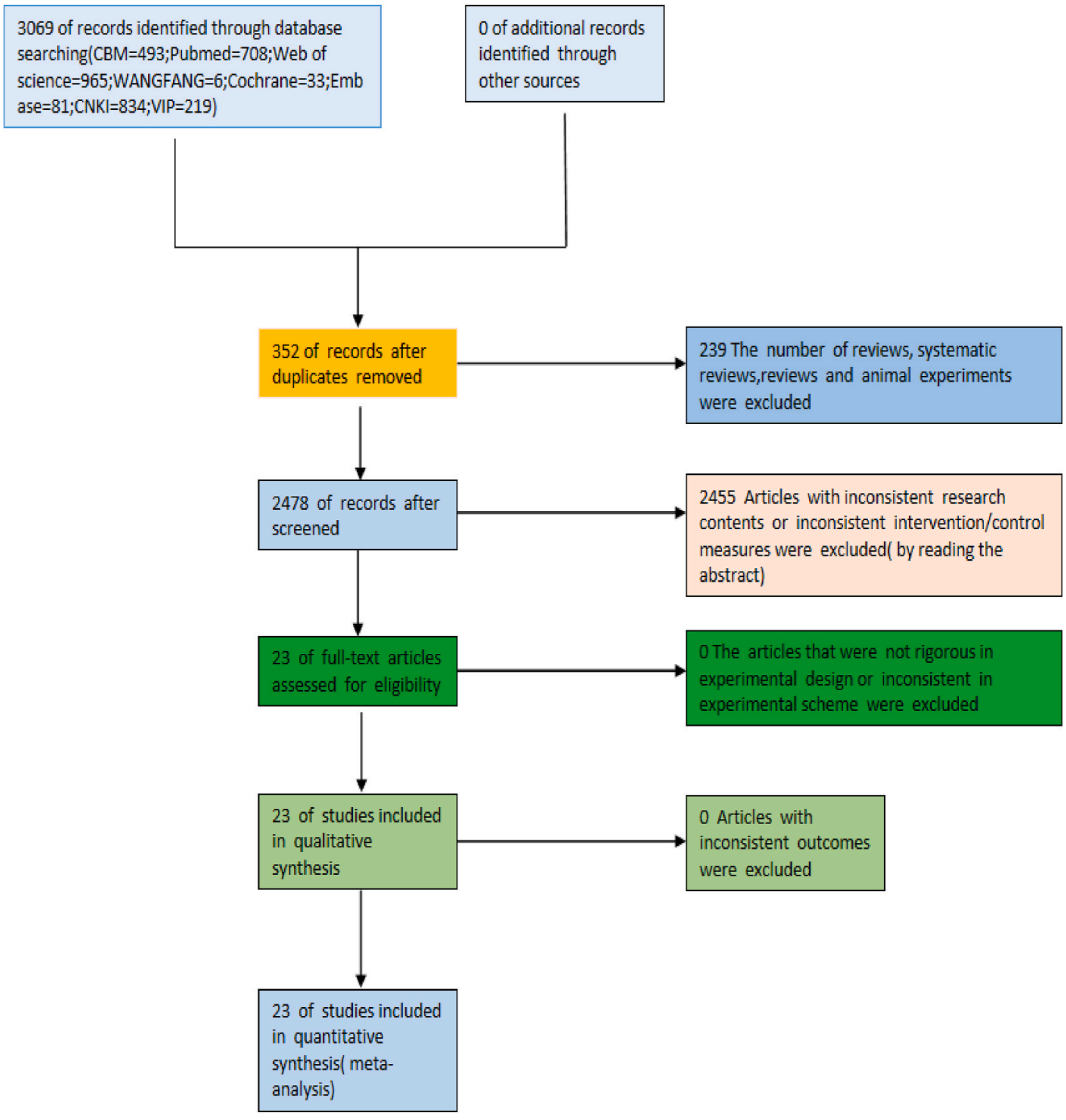

Fig. 1. Flow chart for study selection.

2.4. Exclusion criteria

The exclusion criteria include review, conference papers, systematic evaluation, academic dissertations, animal experiments, republished studies, inability to obtain full text or incomplete data extraction, low literature quality or obvious research defects; Prior to admission, she had suffered from hyperthyroidism, Hashimoto's thyroiditis, subacute thyroiditis and other thyroid related diseases; Previous use of thyroid hormones and antithyroid drugs; Prior I^{131} treatment and thyroid surgery.

2.5. Study selection and data extraction

Literature screening and data extraction Three researchers who have received systematic and evidence-based training independently read, screened and extracted relevant materials according to inclusion and exclusion criteria. Excel was used to input and extract data, and cross-check was conducted after completion. If there was any disagreement, it was decided through discussion or joint consultation with fourth-party researchers. Relevant data of the included literatures were extracted and sorted out, including literature title, first author, publication time, study country (region), sample size, intervention time, evaluation indicators and other information (see Fig. 1).

2.6. Study quality assessment

Literature quality evaluation was carried out by Three researchers who had received systematic and evidence-based training, according to the bias risk assessment method of QuadAS-2 [17], to evaluate the quality of the included literature. In case of different opinions, the quality evaluation was conducted through discussion or joint consultation with fourth-party researchers. Evaluation items include (1) case selection: A. Whether continuous or random cases are included B. Whether the case-control study design was avoided c. Whether the study avoided inappropriate exclusions D. Evaluation of clinical suitability for case selection (2) Trials to be evaluated: a. Whether the results of the trials to be evaluated were interpreted without knowing the results of the Gold standard test B. If A threshold is used, is it predetermined (3) Evaluation of clinical applicability of the test to be evaluated: A. Implementation and

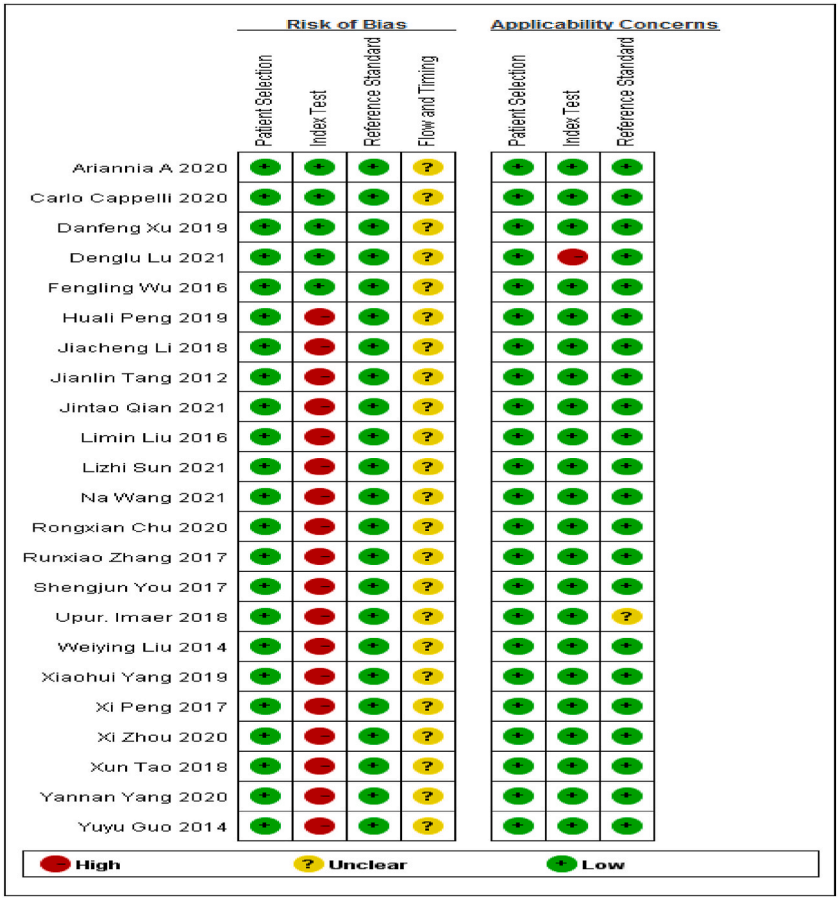

Fig. 2. Summary diagram of the QUADAS 2 bias risk assessment in this study.

interpretation of tests to be evaluated and evaluation of matching of evaluation questions (4) Gold standard: A. Whether the gold standard correctly identifies the target disease states b. Whether blinding was used in the gold standard outcome interpretation (5) Whether blinding was used in the gold standard outcome interpretation: A. Matching of objective conditions defined by gold standard and evaluation questions (5) Case process and progress: A. To be evaluated is there an appropriate time interval between the trial and the gold standard B. are all patients receiving the same gold standard C.Whether all cases were included in the analysis.In this study, two evaluators independently evaluated the methodological quality of the included literatures using quadAS-2, a diagnostic test accuracy quality evaluation tool. The 14 quadAS-2 tools were evaluated as "yes", "no" or "unclear". In Fig. 2, "+" is qualified, "-" is not qualified, and "? "is unclear. Fig. 3 is a bar chart of bias risk assessment. See Figs. 2 and 3 for details.

2.7. Statistical analysis

When studying the value of serum TSH concentration in the diagnosis of differentiated thyroid cancer in patients with thyroid nodules, we searched various databases. In our meta-analysis, we calculated the Spearman correlation coefficients of sensitivity logarithm and (1-specificity) logarithm to evaluate whether there is a threshold effect. We plotted a summary receiver operating characteristic (SROC) curve and calculated the area under the curve. We used sensitivity bias analysis to test the robustness of the data. Meta-Disc 1.4, Stata 15.0, and Review Manager 5.3 were used as statistical software for meta-analysis processing. The diagnostic indicators of heterogeneity between studies were analyzed using the r-test. The heterogeneity source was analyzed using meta-regression analysis. The Spearman correlation coefficient was calculated between sensitivity logarithm and (1-specificity) logarithm to evaluate the presence of a threshold effect. The summary receiver operating characteristic (SROC) curve was plotted to obtain the area under the curve and Q+ index. Funnel plots were drawn using Stata 15.0 software to evaluate publication bias. $P < 0.05$ was considered statistically significant for differences.

2.8. Results

Results 3069 related papers were retrieved for the first time through Chinese and English databases and other channels. 352 duplicate papers were removed by Note Express software, title and abstract were read, 239 reviews, systematic evaluation, reviews and animal experiments were deleted according to inclusion and exclusion criteria, and fulltext links were further obtained. After reading the whole paper, 23 literatures were obtained by excluding 2455 literatures with inconsistent research content or inconsistent intervention/control measures, 0 literatures with inaccurate experimental design or inconsistent experimental scheme, and 0 literatures with inconsistent outcome indicators. A total of 23 literatures were included in the analysis, including 2 English literatures and 21 Chinese literatures.

Basic features of the included literatures a total of 23 literatures were included [18–40], published between 2012 and 2021, and the languages of the included literatures were English and Chinese, including 2 English literatures and 21 Chinese literatures, respectively. A total of 5348 subjects were involved, and the basic characteristics and quality evaluation of the included literature are shown in Table 1.

A total of 23 studies involving 5348 patients were eligible for this study. Elevated serum TSH concentration is an independent risk factor for differentiated thyroid cancer, as well as one of the factors affecting cervical lymph node metastasis. Serum TSH can be used as an auxiliary clinical indicator to judge benign and malignant thyroid nodules. The AUC of TSH detection is 0.79, and the sensitivity and specificity are 0.64 and 0.72.

2.9. Results of data analysis

2.9.1. Heterogeneity test

1. Threshold effect

The data were imported into Meta Disc software for analysis, and the Spearman correlation coefficient between sensitivity logarithm and (1-specificity) logarithm was 0.078 ($P = 0.725 > 0.05$), which was not significant, indicating that there was no threshold

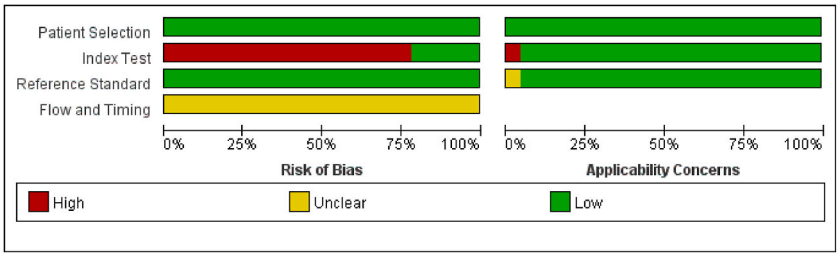

Fig. 3. The QUADAS 2 bias risk assessment bar chart of this study.

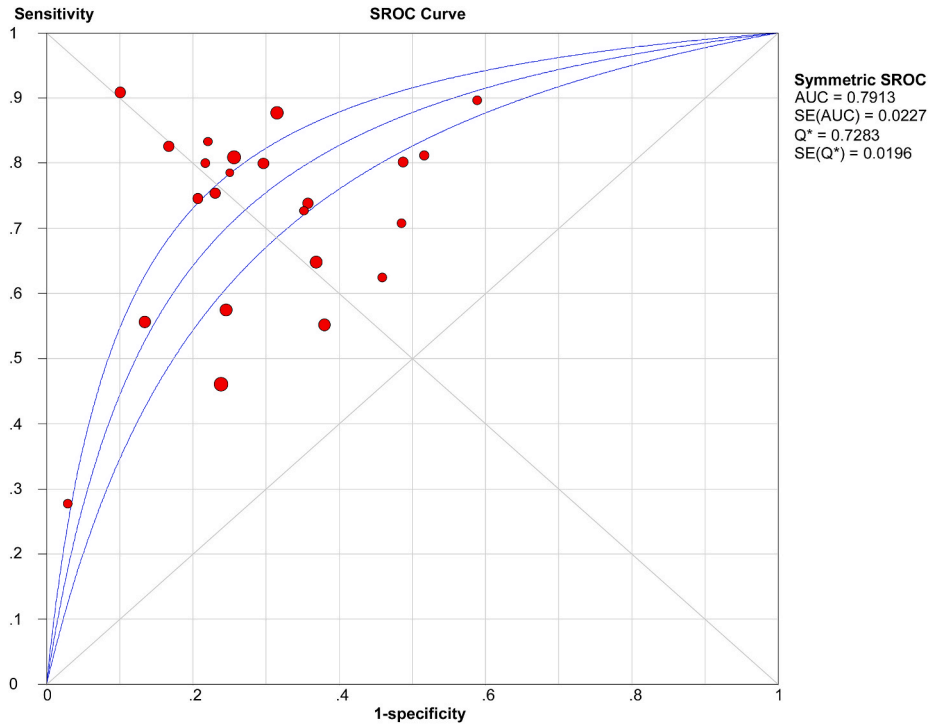

Fig. 4. SROC curve.

Table 1
Characteristics and details of the included studies.

The author	Published time	Sample size (examples)		TSH				The gold standard
		DTC	B	TP	FP	FN	TN	
Denglu Lu [18]	2021	46	174	38	29	8	145	Postoperative pathological
Carlo Cappelli [19]	2020	74	304	48	112	26	192	Postoperative pathological
Ariannia A [20]	2020	20	60	16	13	4	47	Postoperative pathological
Xi Zhou [21]	2020	157	84	116	30	41	54	Postoperative pathological
Upur. Imaer [22]	2018	65	179	52	53	13	126	Postoperative pathological
Fengling Wu [23]	2016	54	35	15	1	39	34	Postoperative pathological
Danfeng Xu [24]	2019	63	121	47	25	16	96	Postoperative pathological
Lizhi Sun [25]	2021	32	48	20	22	12	26	Postoperative pathological
Xun Tao [26]	2018	32	95	26	49	6	46	Postoperative pathological
Na Wang [27]	2021	44	37	32	13	12	24	Postoperative pathological
Yannan Yang [28]	2020	106	39	85	19	21	20	Postoperative pathological
Jintao Qian [29]	2021	221	137	122	52	99	85	Postoperative pathological
Rongxian Chu [30]	2020	88	159	80	16	8	143	Postoperative pathological
Xiaohui Yang [31]	2019	24	66	17	32	7	34	Postoperative pathological
Weiying Liu [32]	2014	30	59	25	13	5	46	Postoperative pathological
Jianlin Tang [33]	2012	28	12	22	3	6	9	Postoperative pathological
Huali Peng [34]	2019	57	139	43	32	14	107	Postoperative pathological
Shengjun You [35]	2017	178	149	99	20	79	129	Postoperative pathological
Limin Liu [36]	2016	90	388	79	122	11	266	Postoperative pathological
Xi Peng [37]	2017	497	126	229	30	268	96	Postoperative pathological
Runxiao Zhang [38]	2017	200	200	115	49	85	151	Postoperative pathological
Jiacheng Li [39]	2018	110	441	89	113	21	328	Postoperative pathological
Yuyu Guo [40]	2014	29	51	26	30	3	21	Postoperative pathological

Note: DTC was Benign, while B was Benign. TP was true positive, FP was false positive, FN was false positive, TN was true negative, and postoperative pathological results were used as the gold standard to judge benign and malignant.

effect in this study. Furthermore, there is no "shoulder arm shape" by drawing symmetrical sROC curve, which further indicates that there is no threshold effect in this study (see Fig. 4).

2. Heterogeneity of non-threshold effects

The Cochran-Q test of the diagnostic odds ratio (DOR) shows that Cochran-Q = 129.35, P < 0.001, indicating that heterogeneity caused by non-threshold effect exists in this study. Furthermore, the sensitivity, specificity, positive likelihood ratio, negative likelihood ratio and I2 of DOR are all greater than 50 %. The above five effect sizes were combined by random effect model (see Fig. 5).

3. Evaluation indexes of diagnostic tests

The combined sensitivity was 0.64 (0.62–0.66), the combined specificity was 0.72 (0.77–0.73), the combined positive likelihood ratio was 2.511 (2.105–2.993), the combined negative likelihood ratio was 0.386 (0.312–0.478), the combined AUC was 0.79 (0.75–0.82), Q index = 0.7283, and the odds ratio of combined diagnosis was 7.14 (4.94–10.30).Shown in Table 2.

2.10. Sensitivity analysis

STATA 15.0 was selected for sensitivity analysis of the data in this study, and the results are as follows:It can be clearly seen from Fig. 6 that 2 original studies have strong sensitivity, while other original studies do not cause sensitivity of calculation results. Overall, the results of this study are relatively stable.

2.11. Published bias test

STATA 15.0 was selected to conduct publication bias test for the data of this study, as shown in Fig. 7:It can be clearly seen from the above results that P > 0.05 means that the funnel plot is symmetrical and there is no publication bias in this study (see Fig. 8).

3. Discussion

Thyroid cancer is a common malignant tumor with a rapid increase in clinical incidence in recent years, papillary thyroid cancer is the type with the highest incidence, and the possibility of early lymph node metastasis is greater, among which the cervical lymph node metastasis rate is the highest, about 21 %–90 % [41,42]. Differentiated thyroid cancer (DTC) is one of the types with prominent clinical manifestations, and related studies have shown that early diagnosis and treatment can effectively improve the survival rate of patients [43]. In recent years, there has been controversy about whether TSH is related to the occurrence and development of thyroid cancer. It is generally believed by scholars that conventional oral levothyroxine can effectively inhibit TSH level and significantly reduce the mortality and recurrence rate of patients in the postoperative treatment of thyroid cancer, indicating that reducing serum TSH level has a positive effect on reducing the incidence of thyroid cancer, thus there is a close relationship between the two [44–47]. Recent studies have confirmed the close correlation between TSH level and thyroid malignant tumor. Wei WEI et al. [48] showed that with the increase of serum TSH concentration, the proportion of PATIENTS with thyroid nodules suffering from DTC increased, and when TSH>4.20 mIU/L, the proportion of PATIENTS with DTC could reach more than 70 %. Zhang Jiangjia et al. [49]. reported that serum TSH level is one of the effective indicators for predicting thyroid cancer, especially for thyroid nodules larger than 10 mm in diameter, which has high reference value. However, Che Weijuan [50] believed that although there are differences in serum TSH levels between benign and malignant thyroid nodules, it is not appropriate to use normal human body reference value as the standard for benign and malignant thyroid nodules, and a more suitable threshold value for screening malignant thyroid nodules should be explored. Guo M ET al [51]. combined serum TSH and ultrasound detection for the diagnosis of thyroid nodule nature, and the results showed that the AUC of TSH detection was 0.651, the AUC of the combined detection was 0.812, and the sensitivity and specificity were 0.851 and 0.782, respectively. However, the ultrasound examination used in this study was mainly qualitative examination. Grey scale score was not used as quantitative basis. Studies have found a close relationship between TSH level and thyroid cancer, and high TSH level can be considered as an independent predictor of thyroid cancer [52].The results of this study showed that the AUC of TSH detection was 0.79, and the sensitivity and specificity were 0.64 and 0.72, respectively. The results of this study indicated that elevated serum TSH concentration was an independent risk factor for differentiated thyroid cancer and one of the factors affecting cervical lymph node metastasis. Serum TSH can be used as an auxiliary clinical indicator for the diagnosis of benign and malignant thyroid nodules. It is expected that the combined application of TSH with other diagnostic methods should be regarded as the direction of future research, so as to provide a stronger evidence-based basis for improving the diagnostic sensitivity of thyroid cancer patients.

In this study, only published Chinese and English literatures were retrieved, and the retrieval of literatures in other languages and grey literatures was insufficient, which may cause certain publication bias. In addition, future studies should evaluate whether TSH in combination with other tests improves diagnostic sensitivity.

Table 2
Evaluation criteria for diagnostic tests.

Detection method	Combined sensitivity (95%CI)	Combined specificity (95%CI)	Combined positive likelihood ratio (95%CI)	Combined negative likelihood ratio (95%CI)	Combined diagnostic odds ratios (95%CI)
Serum TSH	**0.64(0.62–0.66)**	**0.72(0.70–0.73)**	**2.511(2.105–2.993)**	**0.386(0.312–0.478)**	**7.14(4.94–10.30)**

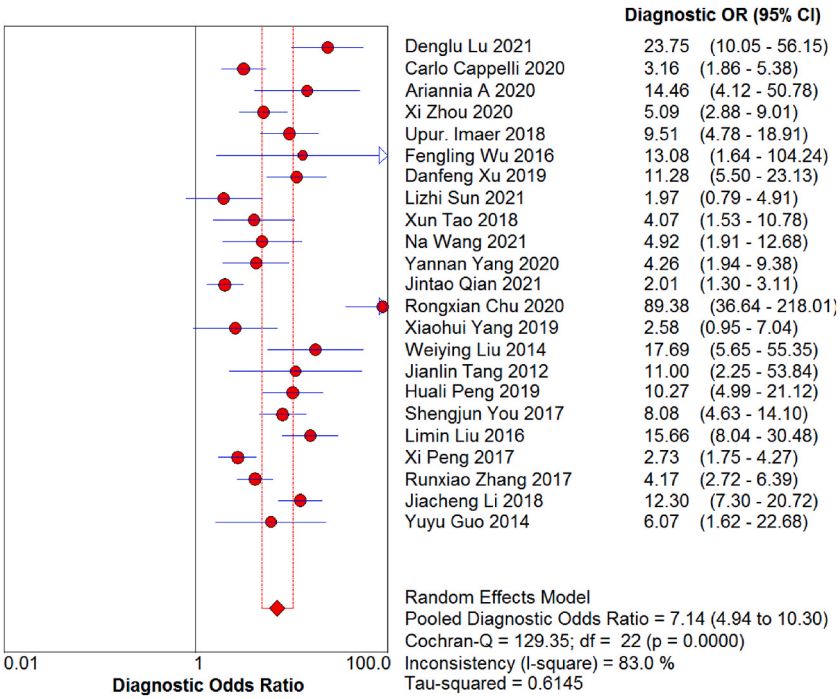

Fig. 5. Diagnostic odds ratio diagram.

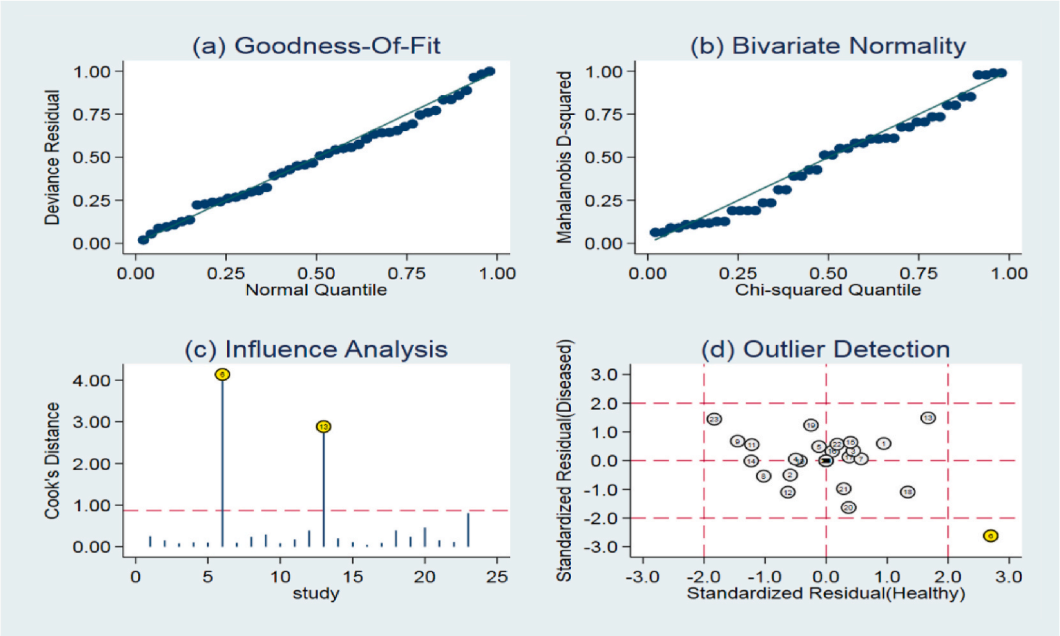

Fig. 6. Sensitivity analysis "From the above figure, it can be clearly seen that there are 2 original studies with strong sensitivity, while other original studies will not cause sensitivity in the calculation results. Overall, this research result is relatively stable."

4. Conclusion

The results of this study suggest that elevated serum TSH concentration is an independent risk factor for differentiated thyroid cancer and also one of the factors affecting cervical lymph node metastasis. Serum TSH can be used as an auxiliary clinical indicator to judge benign and malignant thyroid nodules.

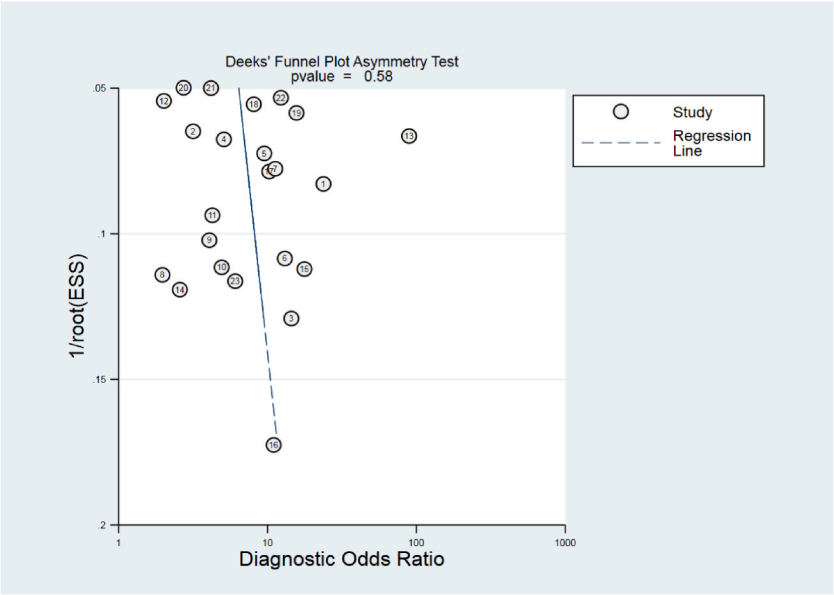

Fig. 7. Published bias test "From the above results, it can be clearly seen that $p > 0.05$, which means that the funnel plot is symmetrical, indicating no publication bias in this study."

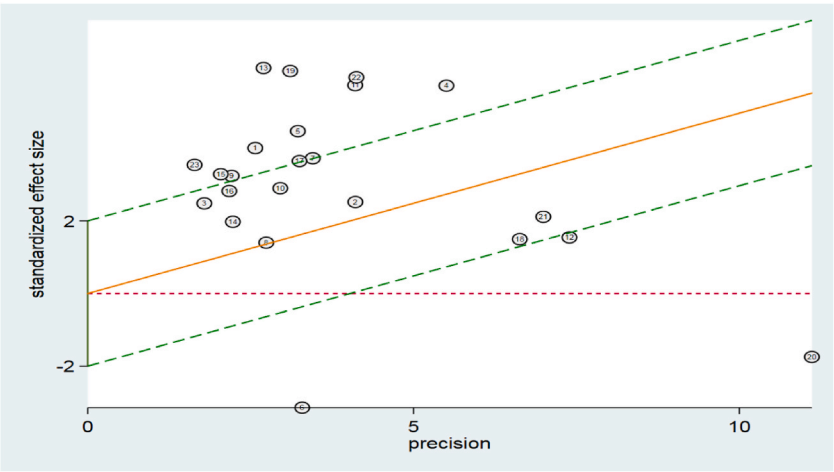

Fig. 8. Galbraith diagram is studied in this paper.

Limitations of this study and implications for future research

Only published Chinese and English literature was retrieved in this systematic evaluation, and there was a lack of retrieval of other languages and grey literature, which may cause a certain publication bias. In addition, future studies should also evaluate how TSH in combination with other tests may improve diagnostic sensitivity.

Funding

This study was funded internally by Sichuan Provincial Department of Science and Technology,No.2022JDKP0037).

Data availability statements

The data that support the findings of this study are available in [repository namel at [PMID/DOI], reference number1-54. These data were derived from the following resources available in the public domain: [CNKI, Wanfang Database, VIP database and China Biomedical Literature Database (CBM), PubMed, Embase, Cochrane Library, Web of Science].

Key messages

The results of this study shows elevated serum TSH concentrations are independent risk factors for the development of differentiated thyroid cancer, is one of the factors that affect transfer analysis, serum TSH can be used as a judgment of thyroid nodules of benign and malignant tumor auxiliary index of clinical application of expectation in the future should apply TSH associated with other diagnosis methods as the research direction of the future, To provide stronger evidence-based basis for improving the diagnostic sensitivity of thyroid cancer patients.

Ethics declarations

Review and/or approval by an ethics committee was not needed for this study because this article is a meta-analysis and does not include any research involving humans or animals.

CRediT authorship contribution statement

Xiao-Yu Fan: Writing – original draft, Methodology, Data curation, Conceptualization. **Wei You:** Writing – review & editing, Project administration, Formal analysis, Data curation, Conceptualization. **Yao Chen:** Software, Resources, Conceptualization. **Chen-Cong Nie:** Software, Project administration, Investigation, Formal analysis. **Xue-Lian Wang:** Validation, Project administration, Methodology. **Cheng Lei:** Validation, Software, Formal analysis, Data curation. **Juan Song:** Validation, Supervision, Software, Data curation. **Huai-Li Luo:** Visualization, Validation, Resources.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Yao Chen reports financial support was provided by Sichuan Provincial Department of Science and Technology (2022JDKP0037). If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

[1] J.J. Wiltshire, T.M. Drake, L. Uttley, et al., Systematic review of Trends in the incidence rates of thyroid cancer, Thyroid 26 (11) (2016) 1541–1552, https://doi.org/10.1089/thy.2016.0100.

[2] B.R. Haugen, E.K. Alexander, K.C. Bible, et al., American thyroid association management guidelines for adult patients with thyroid nodules and differentiated thyroid cancer: the American thyroid association guidelines task force on thyroid nodules and differentiated thyroid cancer, Thyroid 26 (1) (2015) 1–133, https://doi.org/10.1089/thy.2015.0020, 2016.

[3] E. Horvath, S. Majlis, R. Rossi, et al., An ultrasonogram reporting system for thyroid nodules stratifying cancer risk for clinical management, J. Clin. Endocrinol. Metab. 94 (5) (2009) 1748–1751, https://doi.org/10.1210/jc.2008-1724.

[4] J.Y. Park, H.J. Lee, H.W. Jang, et al., A proposal for a thyroid imaging reporting and data system for ultrasound features of thyroid carcinoma, Thyroid 19 (11) (2009) 1257–1264, https://doi.org/10.1089/thy.2008.0021.

[5] Yi-feng Xie, Ying-chang Gao, Hu Xiu tang, Hui-min Zhang, Application value of improved Kwak thyroid imaging report and data system in thyroid nodule diagnosis, Chinese Journal of Medical Innovation 17 (13) (2020) 102–105, https://doi.org/10.3969/j.issn.1674-4985.2020.13.025.

[6] J.Y. Kwak, K.H. Han, J.H. Yoon, et al., Thyroid imaging reporting and data system for US features of nodules: a step in establishing better stratification of cancer risk, Radiology 260 (3) (2011) 892–899, https://doi.org/10.1148/radiol.11110206.

[7] L.X. Yue, Q. Chen, Consensus and problems in thyroid imaging reporting and data system, Journal of Clinical Ultrasound medicine 477 (18) (2016) 185–188, https://doi.org/10.16245/j.cnki.issn1008-6978.2016.03.015, 3.

[8] G. Russ, S.J. Bonnema, M.F. Erdogan, C. Durante, R. Ngu, L. Leenhardt, European thyroid association guidelines for ultrasound malignancy risk stratification of thyroid nodules in adults: the EU-TIRADS, European 4yroid Journal 6 (5) (2017) 225–237.

[9] H. Gharib, E. Papini, D.S. Duick, et al., American association of clinical endocrinologists, associazione medici endocrinologi,and European thyroid association medical guidelines for clinical practice for the diagnosis and management of thyroid nodules: executive summary of recommendations, J. Endocrinol. Invest. 33 (5) (2010) 287–291, https://doi.org/10.3275/7048.

[10] C. Cappelli, I. Pirola, B. Agosti, et al., Complications after fine-needle aspiration cytology: a retrospective study of 7449 consecutive thyroid nodules, Br. J. Oral Maxillofac. Surg. 55 (3) (2017) 266–269, https://doi.org/10.1016/j.bjoms.2016.11.321.

[11] M. Eszlinger, L. Hegedüs, R. Paschke, Ruling in or ruling out thyroid malignancy by molecular diagnostics of thyroid nodules, Best Pract. Res. Clin. Endocrinol. Metabol. 28 (4) (2014) 545–557, https://doi.org/10.1016/j.beem.2014.01.011.

[12] L. Golbert, A.P. de Cristo, C.S. Faccin, et al., Serum TSH levels as a predictor of malignancy in thyroid nodules: a prospective study, PLoS One 12 (11) (2017), https://doi.org/10.1371/journal.pone.0188123. Article IDe0188123.

[13] Y. Nagayama, Thyroid autoimmunity and thyroid cancer-the pathogenic connection: a 2018 update, Horm. Metab. Res. 50 (12) (2018) 922–931, https://doi.org/10.1055/a-0648-4593.

[14] Expert consensus on clinical application of serum markers for thyroid cancer (2017 edition), Chin. J. Clin. Oncol. 45 (1) (2018) 7–13, https://doi.org/10.3969/j.issn.1000-8179.2018.01.265.

[15] L.C. Moeller, D. Fuhrer, Thyroid hormone, thyroid hormone receptors, and cancer: a clinical perspective, Endocr. Relat. Cancer 20 (2) (2013) 19–29, https://doi.org/10.1530/ERC-12-0219.

[16] S.Y. Sohn, H.J. Kim, H.W. Jang, et al., Lack of association between high serum thyroid-stimulating hormone level and risk of papillary thyroid microcarcinomas, Head Neck 36 (1) (2014) 43–46, https://doi.org/10.1002/hed.23252.

[17] P.F. Whiting, A.W.S. Rutjes, M.E. Westwood, et al., QUADAS-2:a revised tool for the quality assessment of diagnostic accuracy studies[J], Ann. Intern. Med. 155 (8) (2011) 529–536, https://doi.org/10.7326/0003-4819-155-8-201110180-00009.

[18] Denglu Lu, Differential diagnostic value of $^{99}Tc^{m}O_4$ radionuclide imaging and serum TSH in ultrasonographically suggested high-risk thyroid nodules, Journal of Guilin Medical College 45 (3) (2021) 147–154, https://doi.org/10.27806/d.cnki.gglyx.2021.000155.

[19] Carlo Cappelli, Ilenia Pirola, Elena Gandossi, et al., Could serum TSH levels predict malignancy in euthyroid patients affected by thyroid nodules with indeterminate cytology? International Journal of Endocrinology 20 (5) (2020) 6–9, https://doi.org/10.1155/2020/7543930.

[20] A. Ariannia, M. Mehrjerdian, et al., Higher TSH level is associated with increased risk of malign ancy in thyroid nodules, J. Pioneer. Med. Sci. 9 (1) (2020) 8–10, https://doi.org/10.1371/journal.pone.0188123.

[21] Xi Zhou, The value of TI-RADS combined with serum TSH in the diagnosis of four types of thyroid nodules, Journal of the University of South China 5 (23) (2022) 9–12, https://doi.org/10.27234/d.cnki.gnhuu.2020.000869.

[22] Upur Imaer, Differential diagnostic value of TSH and TPOAb levels in Hashimoto's thyroiditis and papillary thyroid carcinoma, Journal Of Intractable Diseases 17 (4) (2018) 11–13, https://doi.org/10.3969/j.issn.1671-6450.2018.04.015.

[23] Wu Fengling, The value of conventional gray-scale ultrasound score and serum thyroid-stimulating hormone detection in the diagnosis of solitary thyroid nodules, Prog. Mod. Biomed. 16 (36) (2016) 12–15, https://doi.org/10.13241/j.cnki.pmb.2016.36.042.

[24] Danfeng Xu, Application value of ultrasound elastography and quantitative grading combined with thyrotropin determination in the identification of benign and malignant thyroid nodules, Medical Journal of Air Force 35 (2) (2019) 13–15, https://doi.org/10.3969/j.issn.2095-3402.2019.02.010.

[25] Lizhi Sun, Clinical value of ultrasound elastography combined with serum TSH, TT3 and TT4 in the diagnosis of benign and malignant thyroid nodules, Prog. Mod. Biomed. 21 (5) (2021) 135–137, https://doi.org/10.13241/j.cnki.pmb.2021.05.030.

[26] Xun Tao, The diagnostic value of ultrasound combined with elastography and thyroid stimulating hormone level in benign and malignant thyroid lesions, Military Medical Journal of Southeast China 20 (3) (2018) 15–18, https://doi.org/10.3969/j.Issn.1672-271X.2018.03.003.

[27] Na Wang, The reference value of ultrasonographic features, elastography and serum TSH level in the preoperative diagnosis of differentiated thyroid cancer, Chinese Journal of Endemic Diseases 40 (5) (2021) 15–18, https://doi.org/10.3760/cma.j.cn231583-20201125-00306.

[28] Yannan Yang, Prediction of thyroid stimulating hormone and thyroglobulin on the properties of thyroid nodules, Journal of Wannan Medical College 3 (1) (2020) 131–133, https://doi.org/10.27374/d.cnki.gwnyy.2020.000092.

[29] Jintao Qian, The value of thyroid stimulating hormone in the diagnosis of papillary thyroid carcinoma[J], Journal of Anhui Medical University 6 (30) (2021) 100–103, https://doi.org/10.26921/d.cnki.ganyu.2021.000976.

[30] Rongxian Chu, Diagnostic value of high frequency ultrasound combined with TSH detection in benign and malignant thyroid cystic and solid nodules, Chinese Journal of Gerontology 40 (3) (2020) 133–136, https://doi.org/10.3969/j.issn.1005-9202.2020.21.038.

[31] Xiaohui Yang, TI-RADS-based ultrasonographic refinement scoring method and serum TSH value combined to identify benign and malignant thyroid nodules, J. Bengbu Med. Coll. 44 (6) (2019) 72–75, https://doi.org/10.13898/j.cnki.issn.1000-2200.2019.06.021.

[32] Weiying Liu, The diagnostic value of thyroid radionuclide imaging, serum TSH and ultrasonography in thyroid nodules, J. Isot. 27 (1) (2014) 12–15.

[33] Jianlin Tang, Analysis of diagnosis and treatment of serum TSH in benign and malignant thyroid micronodules, Jilin Medicine 33 (12) (2012) 18–32, https://doi.org/10.13898/j.cnki.issn.1000-2200.2012.33.012.

[34] Huali Peng, Clinical value of combined detection of thyrotropin and thyroglobulin in the diagnosis of benign and malignant thyroid nodules, HEBEI MEDICINE 25 (2) (2019) 95–98, https://doi.org/10.3969/j.issn.1006-6233.2019.02.008.

[35] Shengjun You, The value of preoperative NLR and serum TSH levels in the diagnosis of benign and malignant thyroid nodules, Journal of Fujian Medical University 35 (3) (2017) 12–15, https://doi.org/10.3969/j.issn.1006-6233.2017.03.007.

[36] Limin Liu, The value of preoperative ultrasonography combined with serum TSH level in the diagnosis of thyroid nodules, J. Nanhua Univ. (Med. Ed.) 35 (2) (2016) 85–88, https://doi.org/10.3979/j.issn.1006-6233.2016.03.013.

[37] Xi Peng, The predictive value of preoperative thyroid-stimulating hormone levels in malignant thyroid nodules, J. Sichuan Univ. 4 (48) (2017) 622–625, https://doi.org/10.13464/j.scuxbyxb.2017.04.024.

[38] Runxiao Zhang, Correlation analysis of preoperative serum thyrotropin level combined with Doppler ultrasonography in the diagnosis of differentiated thyroid cancer[J], Journal of Xinjiang Medical University 7 (40) (2017) 888–890, https://doi.org/10.3969/j.issn.1009-5551.2017.07.008.

[39] Jiacheng Li, The role of serum TSH level in the assessment of differentiated thyroid cancer, Chinese Journal of General Surgery Basic and Clinical 25 (8) (2018) 959–963, https://doi.org/10.7507/1007-9424.201801039.

[40] Yuyu Guo, The diagnostic value of serum thyrotropin combined with ultrasonography in benign and malignant thyroid nodules, Journal of Chengdu Medical College 9 (4) (2014) 424–442, https://doi.org/10.3969/j.Issn.16742257.2014.04.012.

[41] J. Jin, R. Machekano, C.R. Mehenry, The utility of preoperative se— rum thyroid—stimulating hormone level for predicting malignant nodular thyroid disease, Am. J. Surg. 199 (2010) 294–297, https://doi.org/10.1016/j.amjsurg.2009.08.028.

[42] Muyuan Liu, Xihong Yang, Haipeng Guo, et al., Characteristics and related factors of cervical lymph node metastasis in thyroid papillary carcinoma of cN1b, Journal of Oncology Research & Clinical 24 (6) (2012) 410–412, https://doi.org/10.3969/j.issn.1674-4136.2012.03.003.

[43] Mingmiao Xue, Mengyuan Shang, Zhihua Wang, Rui Du, et al., Analysis of related factors of cervical lymph node metastasis in differentiated thyroid carcinoma, Chinese Journal of Clinical New Medicine 13 (10) (2020) 362–363, https://doi.org/10.3969/j.issn.1674-3806.2020.10.09.

[44] Wei Wei, Xiaoyun Zeng, Li Zhang, Study on the correlation between serum thyrotropin level and differentiated thyroid carcinoma, Chinese Journal of Endocrinology and Metabolism 29 (5) (2013) 400–402, https://doi.org/10.3760/cma.j.issn.1000-6699.2013.05.012.

[45] S.S. Kim, B.J. Lee, J.C. Lee, et al., Preoperative selLm thyroid stimulating hormone levels in well differentiated thyroid earcinonla is a predictive factor for lateral lymph node metastasis as well as extrathyroida extension in Korean patients:a single center expedence, Endocrine 39 (2011) 259–265, https://doi.org/10.1007/s12020-010-9430-5.

[46] Guo-sheng ren, Xinliang Su, Selection of cervical lymph node dissection for differentiated thyroid carcinoma, Chinese Journal of General Basic and Clinical Medicine 17 (8) (2010) 765–767.

[47] Jianzhou Li, Yongjun Jin, Xin Liu, et al., Correlation between serum thyrotropin level and thyroid cancer, Chin. J. Oncol. 33 (12) (2011) 921–924, https://doi.org/10.3760/cma.j.issn.0253-3766.2011.12.00.

[48] Wei Wei, Xiao-yun Zeng, Li Zhang, Research on the relationship between serum thyroid stimulating hormone level and differentiated thyroid carcinoma, Journal of Endocrinology and Metabolism 7 (5) (2013) 400–402, https://doi.org/10.3760/cma.j.issn.1000-6699.2013.05.012.

[49] Jiang-jia Zhang, Li Yin, Qing-ping Wang, et al., Analysis on the correlation between thyroid stimulating hormone and thyroid papillary carcinoma, Primary Medical Forum 18 (S1) (2014) 187–188, https://doi.org/10.1002/hed.25691.

[50] Wei-juan Che, Thyroid stimulating hormone, thyroid globulin antibody in evaluation of benign and malignant thyroid nodules, Chinese and Western Medical Treatment 35 (1) (2016) 122–123, https://doi.org/10.16662/j.cnki.1674-0742.2016.01.122.

[51] Yu-yu Guo, Ting Gu, Ming-hao Guo, Diagnostic value of serum thyroid stimulating hormone combined with ultrasonography in diagnosis of benign and malignant thyroid nodules, Journal of Chengdu Medical College 9 (4) (2014) 424–427, https://doi.org/10.3969/j.issn.1674-2257.2014.04.012.

[52] H.K. Kim, J.H. Yoon, S.J. Kim, et al., Higher TSH level is a risk factor for differentiated thyroid cancer, Clin. Endocrinol. 78 (3) (2013) 472–477, https://doi.org/10.1111/cen.12027.