Original Article
Diagnostic accuracy of CK-19, Galectin-3 and HBME-1 on papillary thyroid carcinoma: a meta-analysis

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Abstract: The study aimed at evaluating the diagnostic accuracy of cytokeratin 19 (CK-19), Galectin-3 and hector battifora mesothelial antigen-1 (HBME-1) for papillary thyroid carcinoma (PTC). The eligible studies were searched in relevant databases with predefined key searching terms and inclusion criteria. Then, the quality assessment was performed by using Diagnostic Accuracy Studies scoring tool. Following the heterogeneity test, a meta-analysis of pooled several effect size including sensitivity, specificity, positive likelihood ratio (PLR), negative likelihood ratio (NLR) and diagnostic odds ratio (DOR) with their 95% confidence intervals (CIs) were conducted by Meta-DiSc software. Next, the summary receiver operating characteristic ROC (SROC) curve was drawn. Total 29 studies with high quality were included in this meta-analysis. The pooled result of CK-19 showed that sensitivity, specificity, PLR, NLR and DOR were 0.816 (95% CI: 0.799-0.832), 0.872 (95% CI: 0.855-0.888), 5.900 (95% CI: 5.193-6.703), 0.205 (95% CI: 0.185-0.228), respectively. For Galectin-3, the pooled sensitivity, specificity, PLR, NLR and DOR were 0.842 (95% CI: 0.825-0.858), 0.833 (95% CI: 0.814-0.851), 5.057 (95% CI: 4.494-5.690), 0.176 (95% CI: 0.154-0.200) and 33.312 (95% CI: 26.403-42.029). For HBME-1, the pooled sensitivity, specificity, PLR, NLR and DOR were 0.928 (95% CI: 0.913-0.941), 0.864 (95% CI: 0.847-0.880), 6.204 (95% CI: 5.498-7.002), 0.082 (95% CI: 0.067-0.102), 57.107 (95% CI: 43.421-75.107), respectively. The area under curve (AUC) value in SROC curve of CK-19, Galectin-3 and HBME-1 were 0.9134 (95% CI: 0.877-0.950), 0.8452 (95% CI: 0.809-0.882) and 0.9047 (95% CI: 0.868-0.941), respectively. Compared with CK-19 and Galectin-3, HBME-1 was a more accurate maker and might be used independently for PTC diagnosis. CK-19 and Galectin-3 might as second-line detection for PTC diagnosis.

Keywords: Papillary thyroid carcinoma, cytokeratin 19, Galectin-3, hector battiforamesothelial antigen-1, diagnostic accuracy

Introduction

Thyroid cancer is one of most common malignant disease, and papillary thyroid carcinoma (PTC) comprises more than half of thyroid cancer [1]. PTC is the seventh most common cancer in women among the world, and the incidence rate of PTC has increased sharply [2]. Several risk factors have been demonstrated to be related with the increased PTC incidence, such as radiation, thyroid-stimulating hormone levels and iodine intake, body weight, insulin resistance, diet, environmental pollutants, as well as family inheritance [3, 4]. Although the survival rate for PTC is up 90% [5], early diagnosis and treatment of PTC are still important for better prognosis and higher survival rates.

The growth of thyroid nodule is a prominently clinical feature of PTC, and the fine-needle aspiration biopsy (FNAB) is a frequently used method for diagnosing PTC [6]. However, papillary cancers misdiagnosed as benign nodules in the early stage of PTC happens occasionally by using FNAB, and FNAB has limitations for decision making in cellular atypia and suspicious cytology of PTC [7, 8]. In the recent years, the application of molecular diagnosis offers an accurate tool for early diagnosis and heterogeneous group of lesions in PTC [9]. Cytokeratin
Diagnostic value of CK-19, Galectin-3 and HBME-1 on PTC

Data and methods

Materials and methods

Data resources

Eligible studies published in the databases such as Embase (http://www.embase.com) and Pubmed (http://www.ncbi.nlm.nih.gov/pubmed/) up to November, 2016 were searched. The key searching terms were “papillary thyroid carcinoma” OR “thyroid papillary carcinoma” OR “papillary carcinoma of the thyroid” OR “papillary thyroid cancer” OR “papillary adenocarcinoma of thyroid gla” AND Galectin-3 (“Galectin-3” OR “Galectin 3”) AND HBME-1 (“Hector Battifora mesothelial-1” OR “Hector Battiforamesothelial cell-1”) AND CK-19 (Cytokeratin-19). Clinical studies published only in English language were considered.

Inclusion and exclusion criteria

The inclusion criteria were strictly established as follows: (1) The studies were those that evaluated the diagnostic test of CK-19, Galectin-3 or HBME-1 for patients with PTC; (2) The number of binned true positive (TP), false positive (FP), false negative (FN) and true negative (TN) were provided or might be obtained or calculated from other known indicators; (3) In the articles, - or less than 5% were used to indicate negative expression, while +, ++, +++ and ++++ or more than 5% were used for positive expression.

The exclusion criteria for the study were: (1) The study was a review, abstractor report or not a case-control study; (2) The study had the different emphasis in spite of the same research field.

Data extraction and quality assessment

Two investigators independently extracted the data from the included studies, including first author’s name, publication time, research region and time, case numbers of TP, FP, TN and FN on using CK-19, Galectin-3 and HBME-1 for diagnosing PTC. In addition, a quality assessment was performed by using Quality Assessment of Diagnostic Accuracy Studies (QUADAS) tool [15]. The tool contains a series of 14 questions which may be scored with Yes (the information match this item), No (the information does not meet this item) and Unclear (the item is not reported in the study). If there existed divergences during the process of data
abstraction and quality evaluation, disagreements were resolved by discussion with a third assessor to reach a final agreement.

### Statistical analysis

We used the MetaDiSc software (version 1.4) to conduct the diagnostic meta-analysis, and the sensitivity, specificity, PLR, NLR and DOR with their 95% confidence intervals (CIs) were used to measure the effect size. Besides, threshold effect was one of main causes for producing heterogeneity in the diagnostic test, and it was calculated by the spearman correlation coefficient (CC) between specificity and logit sensitivity, and P<0.05 was considered as the cut-off for significance.

Additionally, SROC curve analysis was conducted to evaluate the overall diagnostic effect. Heterogeneity was examined by Q statistic and I² test based on chi-square test [16]. If there exist obviously heterogeneity between the studies (P<0.05 or I²≥50%), the DerSimonian-Laird random effects model was utilized to calculate the pooled effect size. Otherwise, the Mantel-Haenszel fixed effects model was used to calculate the pooled effect size with no significant

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**Table 1. Characteristics of the included studies**

<table>
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<th>HBME-1</th>
<th>CK-19</th>
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<td>+</td>
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<td>-</td>
<td>+</td>
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<td>-</td>
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<td>21</td>
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</table>

Notes: +: positive expression; -: negative expression; PTC: papillary thyroid carcinoma; CK-19: cytokeratin 19; HBME-1: hector battiforamesothelial antigen-1.
Diagnostic value of CK-19, Galectin-3 and HBME-1 on PTC

Table 2. Quality assessment of the included studies

<table>
<thead>
<tr>
<th>Studies</th>
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</tbody>
</table>

Notes: QUADAS: Quality Assessment of Diagnostic Accuracy Studies. +: YES; -: NO; 0: Not clear. 1. Was the spectrum of patients representative of the patients who will receive the test in practice? 2. Were selection criteria clearly described? 3. Is the reference standard likely to correctly classify the target condition? 4. Is the time period between reference standard and index test short enough to be reasonably sure that the target condition did not change between the two tests? 5. Did the whole sample or a random selection of the sample, receive verification using a reference standard of diagnosis? 6. Did patients receive the same reference standard regardless of the index test result? 7. Was the reference standard independent of the index test (i.e. the index test did not form part of the reference standard)? 8. Was the execution of the index test described in sufficient detail to permit replication of the test? 9. Was the execution of the reference standard described in sufficient detail to permit its replication? 10. Were the index test results interpreted without knowledge of the results of the reference standard? 11. Were the reference standard results interpreted without knowledge of the results of the index test? 12. Were the same clinical data available when test results were interpreted as would be available when the test is in practice? 13. Were uninterpretable/intermediate test results reported? 14. Were withdrawals from the study explained?

Results

Based on the searching strategies, total 559 studies (PubMed: 176; Embase: 383) were searching after the preliminary selection from both PubMed and Embase databases. Then, 116 repetitive articles were found and eliminated, and 369 irrelevant studies were removed via reading the titles and abstracts. Following further selection, another 45 studies without concrete data or with the repeated study sites were excluded. Finally, a total of 29 studies conformed to all the inclusion criteria were obtained [18-46] (Figure 1).

As shown in Table 1, the published data of the included articles were from 2001 to 2016, and the studies were from different countries such as USA, Japan, Turkey, Canada, South Korea, Italy, Egypt, Malaysia and China. Moreover, a total of 4455 participants were included in this meta-analysis.

Quality assessment of the selected studies

The QUADAS scoring system was performed to assess the quality of the 29 selected studies. As shown in Table 2, a majority of studies were conformed to larger than nine of the 14 described criteria, showing that the quality of studies were relatively high. Summary scores were not calculated, since the interpretation can be problematic and potentially misleading.

Quantitative data pooling

In this meta-analysis, based on the MetaDiSc software, the pooled effect size of sensitivity, specificity, PLR, NLR and DOR of diagnostic indicators of CK-19, Galectin-3 and HBME-1 on PTC was calculated.
Diagnostic value of CK-19, Galectin-3 and HBME-1 on PTC

A total of 20 included studies were related to the diagnosis value of CK-19 for PCT [19-27, 31, 33-35, 37, 39, 40, 42, 44-46], and remarkably heterogeneity were detected between the studies (sensitivity: P<0.01, I²=91.4%; specificity: P<0.01, I²=88.5%; PLR: P<0.01, I²=87.7%; NLR: P<0.01, I²=90.7%; DOR: P<0.01, I²=83.5%). Thus, the DerSimonian-Laird random effects model was chosen to combine the pooled effect value of sensitivity, specificity, PLR, NLR and DOR between above studies due to the significant heterogeneity (sensitivity: P<0.01, I²=86.8%; specificity: P<0.01, I²=85.5%; PLR: P<0.01, I²=85.5%; NLR: P<0.01, I²=84.4%; DOR: P<0.01, I²=70.7%). The pooled value of sensitivity was 0.842 (95% CI: 0.825-0.858, Figure 4A), specificity was 0.833 (95% CI: 0.814-0.851, Figure 4B), PLR was 5.057 (95% CI: 4.494-5.690), NLR was 0.176 (95% CI: 0.154-0.200) and DOR was 33.312 (95% CI: 26.403-42.029), respectively.

In addition, there was no statistical significance for the threshold effect (P=0.7606), and SROC curve showed symmetrical. Therefore, a Man-
Diagnostic value of CK-19, Galectin-3 and HBME-1 on PTC

The tel-Haenszel fixed effects model was used for the statistical analysis. The pooled AUC was 0.9128 (95% CI: 0.880-0.946) and the Q index was 0.8452 (95% CI: 0.809-0.882, Figure 5).

HBME-1

Twenty-one studies were involved in assessing the diagnostic value of HBME-1 for RTC [18-20, 22-27, 29, 33-37, 39, 40, 43-46], and the obviously heterogeneity were detected between those studies for each effect size including sensitivity, specificity, PLR, NLR and DOR. Thus, we selected the DerSimonian-Laird random effects model to calculate those pooled effect size. The result showed that pooled sensitivity was 0.928 (95% CI: 0.913-0.941; P<0.01, $I^2=71.1%$; Figure 6A), specificity was 0.864 (95% CI: 0.847-0.880; P<0.01, $I^2=84.7%$; Figure 6B), PLR was 6.204 (95% CI: 5.498-7.002; P<0.01, $I^2=88.5%$), NLR was 0.082 (95% CI: 0.067-0.102; P<0.01, $I^2=79.7%$) and DOR was 57.107 (95% CI: 43.421-75.107; P<0.01, $I^2=82.8%$), respectively. Additionally, through performing the threshold effect test between the studies, no striking significance were examined (P=0.7682), and the Mantel-Haenszel fixed effects model was chosen for the statistical analysis. As a result, the summary AUC was 0.9601 (95% CI: 0.935-0.985) and the Q index was 0.9047 (95% CI: 0.868-0.941, Figure 7).

Discussion

In the present study, total 29 studies were used to evaluate the diagnostic accuracy of CK-19, Galectin-3 and HBME-1 for PTC. According to the criterion, PLR>10 or NLR<0.1 of the molecular marker can be considered as an independent diagnostic indicator, and DOR>25 is considered as moderately accurate and >100 is considered as highly accurate [47]. Our results showed that the moderate PLR (5.900), moderate NLR (0.205) and moderate DOR (30.024) of CK-19, and moderate PLR (5.057), moderate NLR (0.176) and moderate DOR (33.312) of Galectin-3 did not meet the criterion to be as independent diagnostic indicators for PTC. However, CK-19 and Galectin-3 might act as second-line detection due to their value of sensitivity, specificity, AUC and Q index of CK-19 and Galectin-3 were both high with more than 0.810, suggesting a high accuracy of CK-19 and Galectin-3 in diagnosis of PTC. Notably, HBME-1 might act as independent diagnostic maker with the NLR value (0.082) was less than 0.1. Additionally, the pooled value of PLR (6.204), sensitivity (0.928), specificity (0.864), DOR (57.107), AUC (0.9601) and Q index (0.9047) of HBME-1 were the maximum among those three makers.

Although our results showed that CK-19 and Galectin-3 could not be independently used to detect PTC from benign nodes, they also had certain diagnostic value for PLR. Reportedly, CK-19 is positive expression in papillary carcinomas, but not high expression or negative expression in papillary hyperplasia [48]. In addition, it has been proved that CK-19 can distinguish the follicular variant of papillary carcinoma from other follicular thyroid tumor [49]. Htwe et al have provided that an obviously overexpressed level of Galectin-3 is detected in PTC cells versus the neighboring normal matrix.
Diagnostic value of CK-19, Galectin-3 and HBME-1 on PTC

Figure 4. Diagnostic analysis of papillary thyroid carcinoma using Galectin-3. A: Sensitivity; B: Specificity.

Additionally, our result showed that HBME-1 could be independently used for diagnosing PTC with high sensitivity, AUC and low NLR. In addition, HBME-1 immunostaining is beneficial for differentiating PTC tissues from benign thyroid tissues [53]. Similarly, Dencic et al have observed that diffuse, tall cell and solid PTC variants are respectively presented 100%, 66.67% and 56.52% as HBME-1 positive immunoreaction, and they recommend using HBME-1 to enhance the diagnostic rate of most PTC variants [54]. Besides, it has been reported that HBME-1 has high sensitivity (94.5%) and moderate specificity (77.08%) for diagnosing PTC [14]. Interestingly, the sensitivity, specificity and positive predictive value are respectively 100%, 92.9% and 0.9 by only using HBME-1 as single discriminator between PTC and goitrous nodules, and uniting HBME-1 and CK-19 is up to 100%, 100% and 1 [55].

Among CK-19, Galectin-3 and HBME-1, HBME-1 was the best choice. It was consistent with another study which has evaluated the thyroid tumor markers of CK-19, Galectin-3 and HBME-1, they have indicated HBME-1 is most accurate to act as a single maker for PTC, but they also have proposed that Galectin-3 may be served as a single maker for PTC [56]. The sample size might be the cause for this difference, and our sample size was larger. In addition, there were several limitations in the present study. At first, there were significant heterogeneities in each effect size which might be caused by different sampling conditions and detection methods. However, we failed to perform subgroup analyses by these factors, since the data were insufficient. Second, the popula-
Diagnostic value of CK-19, Galectin-3 and HBME-1 on PTC

tions of the included studies were not unified, and they were from different countries including China, Egypt, South Korea, Turkey, Canada, American, Malay-sia, Japan, Italy and Serbia, which might lead to bias. Third, the sample size were still needed to add to attenuate the statistical difference and improve the reliability of the results. Therefore, more studies involving large samples and detailed demographic information may be needed to provide potent evidence. However, our study was still of great value, since our included samples were at most in the same type of research to systematically evaluate the diagnostic accuracy of CK-19, Galectin-3 and HBME-1.

HBME-1 might be used as single discriminator for PCT diagnosis, and CK-19 and Galectin-3 might also have important diagnostic value for PCT.

Disclosure of conflict of interest

None.

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References

[1] Yun JY, Kim YA, Choe JY, Min H, Lee KS, Jung Y, Oh S and Kim JE. Expression of cancer stem cell markers is more fre-
Diagnostic value of CK-19, Galectin-3 and HBME-1 on PTC

Figure 7. SROC curve for papillary thyroid carcinoma using hector batto- 
foramesothelial antigen-1 (HBME-1). SROC: Summary receiver operating 
characteristic; AUC: Area under curve.

quent in anaplastic thyroid carcinoma com-
pared to papillary thyroid carcinoma and is re-
lated to adverse clinical outcome. J Clin Pathol 
and Vigneri R. Worldwide increasing incide-
nce of thyroid cancer: update on epidemiology 
and risk factors. J Cancer Epidemiol 2013; 
2013: 965212-965212.
roid carcinoma. J Surg Oncol 2006; 94: 719-
724.
[5] Mazzaferri EL. An overview of the manage-
ment of papillary and follicular thyroid car-
[6] Pelizzo MR, Merante Boschini I, Toniato A, Pag-
etta C, Casal Ide E, Mian C and Rubello D. 
Diagnosis, treatment, prognostic factors and 
long-term outcome in papillary thyroid car-
icoma. Minerva Endocrinol 2008; 33: 359-
379.
[7] Das DK and Sharma PN. Diagnosis of papillary 
thyroid carcinoma in fine needle aspiration 
smears: factors that affect decision making. 
[8] Ito Y, Higashiyama T, Takamura Y, Miya A, Ko-
abayashi K, Matsuzuka F, Kuma K and Miyauchi 
A. Long-term follow-up for patients with papil-
lar thyroid carcinoma treated as benign nod-
[9] Kato MA and Fahey TJ. Molecular markers in 
thyroid cancer diagnostics. Surgical Clinics of 
North America 2009; 89: 1139-1155.
QC and Wang DT. Expression 
of RET, cytokeratin 19,TG and 
Ki-67 in papillary thyroid carci-
noma. Chinese Journal of Clini-
cal & Experimental Pathology 
MA, Donner DB, Bertagnolli 
MM, Moore FD Jr and Ruan DT. 
Galectin-3 regulates apoptosis 
and doxorubicin chemoresis-
tance in papillary thyroid can-
cer cells. BiochemBiophys Res 
[12] Pisani T, Vecchione A and Gio-
vagnolii MR. Galectin-3 immu-
nodetection may improve cyto-
logical diagnosis of occult pa-
pillary thyroid carcinoma. Anti-
[13] Krenács L, Tóthilépták J, Demete-
ter J, Piukovics K, Borbényi Z, 
Gogolák P, Sári E and Bagdi E. Monoclonal 
antibody HBME-1 reacts with a minor subset 
of B cells with villous surface and can be 
useful in the diagnosis of hairy cell leukemia 
and other indolent lymphoproliferations of 
villos B lymphocytes. Virchows Arch 2013; 
463: 787-794.
[14] Chen YJ, Zhao RM, Zhao Q, Li BY, Ma QY, Li X 
and Chen X. Diagnostic significance of elevat-
ed expression of HBME-1 in papillary thyroid 
and Kleijnen J. The development of QUADAS: a 
tool for the quality assessment of studies of 
diagnostic accuracy included in systematic 
[16] Lau J, Ioannidis JP and Schmid CH. Quan-
titative synthesis in systematic reviews. AnnIntern 
Med 1997; 127: 820-826.
[17] Zamora J, Abraira V, Muriel A, Khan K and 
Coomarasamy A. Meta-DiSc: a software for 
meta-analysis of test accuracy data. BMC Med 
[18] Raouf AE and Ibrahim TR. Immunohistochemi-
cal expression of HBME-1 and galectin-3 in the 
differential diagnosis of follicular-derived thy-
roid nodules. Pathol Res Pract 2014; 210: 971-
978.
[19] Atik E, Guray M,unesacar R, Ozgur T and 
Canda T. Immunohistochemical analysis of thy-
roid follicular neoplasms and BRAF mutation 
correlation. Indian J Cancer 2014; 51: 63-68.
[20] Barut F, Kandemir NO, Bektaş S and Bahadır 
B. Universal markers of thyroid malignancies: 
galectin-3, HBME-1, and cytokeratin-19. End-
Diagnostic value of CK-19, Galectin-3 and HBME-1 on PTC


Diagnostic value of CK-19, Galectin-3 and HBME-1 on PTC


