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Recent Research Advances in Diagnostic Models for Papillary Thyroid Carcinoma

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Abstract

Papillary thyroid carcinoma (PTC) is the most common pathological type of thyroid cancer, and its accurate diagnosis is crucial for treatment planning and prognostic evaluation. In recent years, rapid advancements in high-throughput sequencing, radiomics, and artificial intelligence have facilitated a shift in PTC diagnosis from traditional empirical judgment toward multidimensional data-driven precision approaches. This article systematically reviews recent progress in diagnostic models for PTC, with a focus on methodologies constructed using ultrasound imaging features, molecular biomarkers, and multimodal data integration. The technical strengths, clinical applicability, and current limitations of various models are analyzed. Furthermore, this review discusses future directions in PTC diagnostic model research, aiming to provide valuable insights for clinical diagnosis and related studies.

Keywords: Papillary thyroid carcinoma; diagnostic model; molecular biomarkers; multimodal integration.

1. Introduction

Thyroid cancer is one of the most rapidly increasing malignancies worldwide, with papillary thyroid carcinoma (PTC) accounting for over 80% of all thyroid cancer cases [1]. The incidence of PTC has been rising globally in recent years [2, 3]. Although most PTC patients have a favorable prognosis, clinical diagnosis still faces multiple challenges, including accurate differentiation between benign and malignant thyroid nodules, early prediction of lymph node metastasis, and precise detection of molecular features such as the BRAF V600E mutation. Conventional diagnostic methods, including ultrasonography and fine-needle aspiration (FNA) biopsy, are widely used in clinical practice but are limited by operator subjectivity, invasiveness, and high false-negative rates [4].

In recent years, rapid advances in high-throughput sequencing, radiomics, and artificial intelligence (AI) technologies have facilitated a shift in PTC diagnosis from empirical judgment toward data-driven precision medicine. This article systematically reviews the latest research

progress in PTC diagnostic models based on multimodal data and discusses future directions in the field.

2. Ultrasound-Based Diagnostic Models

2.1 Conventional Ultrasound and C-TIRADS Guidelines

Ultrasonography is the preferred method for thyroid nodule screening and diagnosis due to its non-invasive nature and operational convenience. Conventional ultrasound differentiates benign from malignant nodules by evaluating morphological features such as hypoechogenicity, ill-defined margins, microcalcifications, and a taller-than-wide shape. Cen Xiaowen (2024) [1,5] developed an auxiliary diagnostic model for thyroid cancer by integrating the C-TIRADS guidelines with ultrasound feature analysis. This model systematically evaluates thyroid nodules through differential analysis of various sonographic features in combination with C-TIRADS classification criteria. The results demonstrate that the model exhibits high sensitivity and specificity in discriminating benign and malignant nodules, significantly improves the detection rate of thyroid cancer, reduces unnecessary fine-needle aspiration (FNA) biopsies, and provides a more reliable tool for precise clinical assessment of nodule nature. Similarly, Song et al. [6,7] found that combining color Doppler ultrasound with thyroid autoantibody testing enhances the diagnostic accuracy of early-stage thyroid cancer.

2.2 Ultrasound Radiomics and Artificial Intelligence Models

Ultrasound radiomics involves the high-throughput extraction of quantitative features (e.g., texture and morphological characteristics) from ultrasound images and the construction of diagnostic models using machine learning algorithms. This approach overcomes the limitations of conventional methods that rely on visual inspection and empirical judgment, offering a more objective and in-depth quantitative basis for diagnosis. Tang Jiajia (2024) conducted a study on the application of this model in diagnosing differentiated thyroid carcinoma. A large number of radiomic features, including texture and morphological characteristics, were extracted from ultrasound images, and machine learning algorithms were employed for feature selection and model construction. In the validation set, the model achieved high levels of diagnostic accuracy, sensitivity, and specificity, demonstrating strong potential for clinical application [8]. Furthermore, the automatic analysis and diagnostic capabilities of artificial intelligence in interpreting ultrasound images substantially improve diagnostic efficiency and effectively reduce the impact of human factors.

3. Diagnostic Models Based on Molecular Biomarkers

3.1 miRNA and Proteomic Biomarkers

MicroRNAs (miRNAs) are a class of endogenous non-coding small RNAs that play important

roles in the regulation of gene expression. Recent studies have revealed significant dysregulation of multiple miRNAs in both tissue and serum of papillary thyroid carcinoma (PTC) patients, highlighting their potential as diagnostic biomarkers. Among them, miRNAs such as miR-221 and miR-222 are upregulated in PTC, while miR-146b and miR-204 are downregulated. These expression changes are closely associated with the development and progression of PTC.

Wang Meiling (2024) conducted a study on the construction of a serum miRNA-based diagnostic model for PTC. By analyzing miRNA expression profiles in the serum of PTC patients and healthy controls, a panel of differentially expressed miRNAs was identified and used to develop a diagnostic model [4]. This model demonstrated strong diagnostic performance in both training and validation sets, effectively distinguishing PTC patients from healthy individuals, thereby offering a promising non-invasive diagnostic approach. Furthermore, studies by Sun Kehuan [9] and Lu Xiubo et al. [10] indicated that serum and salivary proteomic analyses could provide specific diagnostic biomarkers for PTC, though their clinical applicability requires further validation.

3.2 Diagnostic Models Based on Methylation Biomarkers

DNA methylation plays a critical role in tumorigenesis. Zhang Jiali (2024) compared genome-wide methylation profiles between PTC tissues and normal thyroid tissues, identifying a series of differentially methylated sites significantly associated with PTC [11]. A diagnostic model constructed based on these methylation sites demonstrated high accuracy in distinguishing PTC from normal tissue, providing novel molecular markers for early PTC diagnosis.

Hong et al. [12,13] further developed a PTC diagnostic model based on circulating free DNA (cfDNA) methylation, showing high potential for clinical translation. A research team led by Professor Xiao Haipeng from the First Affiliated Hospital of Sun Yat-sen University published a study in eBioMedicine in which they utilized techniques such as reduced-representation bisulfite sequencing to construct a methylation marker panel based on cfDNA. The study enrolled 408 patients with thyroid nodules and, through a multi-phase design, established the ThyMet assay comprising 98 methylation markers. Finally, a classifier with six markers was developed, achieving a sensitivity of 71.2% and specificity of 78.8% in discriminating PTC from benign thyroid nodules. When combined with ultrasonography, the integrated ThyMet-US prediction model demonstrated even better performance, with an AUC as high as 0.992 in the training set.

3.3 Genetic Testing and Multi-Gene Diagnostic Models

Genetic testing plays a significant role in the diagnosis of papillary thyroid carcinoma (PTC), with the BRAF V600E mutation—the most common genetic alteration in PTC—being closely associated with tumor aggressiveness and risk of recurrence. A study by Sun Peng (2024) investigated the utility of combining ultrasonography, CT, and BRAF V600E testing in the preoperative evaluation of cervical lymph node metastasis in PTC. The results demonstrated that this integrated approach significantly improved the predictive accuracy for lymph node metastasis,

providing critical guidance for clinical treatment planning [14].

With advances in molecular diagnostic technologies, multi-gene testing has been increasingly applied in PTC diagnosis. Liu Shiqiang (2024) developed a predictive model by analyzing the correlation between multi-gene expression profiles and lateral cervical lymph node metastasis in PTC. This model comprehensively evaluates the expression levels of multiple genes, enabling more accurate assessment of the risk of lateral cervical lymph node metastasis and thereby offering more targeted guidance for clinical management [15].

4. Diagnostic Models Based on Clinical Features and Multimodal Integration

4.1 Clinical Feature-Based Diagnostic Models

Clinical features of papillary thyroid carcinoma (PTC), including patient age, gender, tumor size, capsular invasion, and lymph node metastasis, hold significant value in disease diagnosis and prognostic evaluation. These indicators not only reflect the biological behavior of tumors but also provide critical evidence for clinical decision-making. Xiao Siqi et al. (2024) [16] specifically investigated the role of preoperative assessment factors in predicting intermediate- to high-risk PTC, systematically analyzing the correlation between various factors and disease risk [17,18].

Through retrospective analysis of a large number of clinical cases, factors closely associated with intermediate- to high-risk PTC—such as age, tumor size, and capsular invasion—were identified and used to construct a predictive model. This model demonstrated high accuracy in predicting intermediate- to high-risk PTC, enabling clinicians to more precisely evaluate disease status preoperatively and formulate individualized treatment plans, thereby potentially improving patient outcomes.

4.2 Machine Learning-Based Risk Assessment Model Using Multidimensional Data

A research team led by Professor Luo Dingcun from Hangzhou First People's Hospital published a study in the International Journal of Surgery in which they employed machine learning methods to develop a Preoperative Risk Assessment Classifier for PTC (PRAC-PTC) by integrating four-dimensional information: proteomic, genetic, immunologic, and clinical data. The study collected 558 PTC clinical samples, and multicenter validation showed that the diagnostic performance of PRAC-PTC surpassed that of senior clinicians. When assisting clinicians in risk assessment, the classifier improved diagnostic accuracy by 24.6% and 25.6%, respectively.

4.3 Multimodal Data Integration-Based Diagnostic Models

Given the limitations of single diagnostic indicators in achieving comprehensive and accurate diagnosis of PTC, the integration of multimodal data to construct diagnostic models has become a major research focus. Such multimodal data encompass ultrasound imaging, molecular biomarkers, and clinical indicators. By synergistically analyzing diverse data sources, these models leverage the strengths of each data type, thereby enhancing diagnostic accuracy and reliability.

A representative example is the preoperative diagnostic prediction model for thyroid cancer developed by Gao Mengyang (2023) [19,20], which integrated multimodal data including clinical indicators and ultrasound imaging features using machine learning algorithms. Validation results demonstrated that the diagnostic accuracy of this model significantly outperformed methods relying on single indicators, highlighting the superiority of multimodal data integration. Similarly, Wang Zike (2022) [21] confirmed that integrating multimodal information—such as clinical data, ultrasound images, and molecular biomarkers—can effectively improve the diagnostic efficacy for PTC. The diagnostic model constructed in that study exhibited excellent performance in distinguishing PTC from benign thyroid nodules.

Further supporting this approach, Xi et al. [22,23] demonstrated that machine learning models can dynamically optimize variable weights and adapt to different population characteristics (e.g., variations in iodine intake levels), laying the foundation for personalized diagnosis. Additionally, Yu Youlin et al. [24,25] developed a diagnostic model combining plasma cfDNA and ultrasound features, which showed high diagnostic performance in an independent validation set. Tang Zhongwei et al. [26] constructed a combined diagnostic model incorporating "ultrasound features + inflammatory markers + TSH," which demonstrated superior diagnostic efficacy in PTC, particularly in discriminating cases with atypical ultrasound presentations. The sensitivity of this model was significantly higher than that of traditional methods.

These studies provide valuable insights for PTC diagnosis, not only confirming the advantages of multimodal data integration but also establishing a theoretical foundation for developing more precise diagnostic tools in the future. With continuous advancements in artificial intelligence technology, multimodal data-based diagnostic models for PTC are expected to play an increasingly important role in clinical practice.

5. Research Trends and Future Directions

5.1 Deep Integration of Artificial Intelligence and Radiomics

With the rapid advancement of artificial intelligence (AI), its application in medical imaging continues to deepen. In the future, the deep integration of AI and radiomics will be a critical direction for the development of PTC diagnostic models. Deep learning algorithms can uncover deeper-level features in medical images such as ultrasound, CT, and MRI, enabling more accurate

diagnosis of PTC. Additionally, AI can facilitate automatic image analysis and report generation, significantly improving diagnostic efficiency and reducing human error.

Furthermore, AI technology is expected to integrate multi-source data, including molecular diagnostics and clinical information, to construct more comprehensive and precise diagnostic models for PTC. Such multimodal integrated approaches can not only enhance diagnostic accuracy but also provide robust support for personalized treatment planning, advancing PTC diagnosis and treatment to a higher level.

5.2 Integration and Application of Multi-Omics Data

Beyond widely studied molecular markers such as miRNAs, DNA methylation, and genetic testing, the integration and application of multi-omics data are emerging as a new research direction in PTC. The three-dimensional integration of "imaging-molecular-clinical" data will become a key focus [14,27,28].

The in-depth integration of multi-omics data opens new avenues for the clinical management of PTC. By comprehensively analyzing multi-omics data from PTC patients, researchers can identify biomarker combinations with superior diagnostic performance. These combined biomarkers can not only improve the accuracy of PTC diagnosis but also predict disease progression, prognosis, and sensitivity to specific treatments, providing a scientific basis for individualized therapeutic decisions.

5.3 Extending from Diagnosis to Prognostic Prediction and Treatment Guidance

While current AI-based diagnostic models primarily focus on the differential diagnosis of PTC, future efforts should aim to develop models for prognostic prediction and recurrence monitoring [15,29]. Prognostic models can assist clinicians in more accurately evaluating patient outcomes and informing personalized treatment strategies. By integrating multidimensional information such as genetic characteristics, clinicopathological features, and treatment responses, predictive models can effectively forecast key prognostic indicators including recurrence risk and survival rates. Based on diagnostic results and prognostic predictions, more targeted treatment guidance—such as determining optimal surgical approaches or the need for adjuvant therapy—can be provided to patients, ultimately improving treatment efficacy and quality of life.

5.4 Clinical Translation and Application

Although significant progress has been made in PTC diagnostic models, most achievements remain at the laboratory stage, and their clinical translation and practical application face numerous challenges. To advance this field, future research should focus on the following aspects: First, developing specialized models for different clinical needs—for instance, low-cost, high-sensitivity models for primary screening, and high-accuracy models for predicting metastasis to guide surgical decisions [16,30]. Second, addressing standardization issues to enhance the generalizability and reproducibility of models across different medical institutions and detection

platforms. Finally, specialized training for clinicians to improve their understanding and application of novel diagnostic models is crucial for successful clinical implementation.

6. Conclusion

Significant progress has been made in PTC diagnostic models, particularly in ultrasound imaging, molecular biomarker detection, and multimodal integration, broadening the pathways to improve diagnostic accuracy. These models demonstrate strong potential for clinical application but also exhibit limitations: the diagnostic accuracy and reliability of some models require further validation, and challenges remain in clinical translation and practical implementation. In the future, with rapid advancements in AI technology and further research, PTC diagnostic models will evolve toward greater precision, comprehensiveness, and intelligence. These technological improvements are expected to provide more reliable support for early screening, precise subtyping, prognostic assessment, and individualized treatment decisions, ultimately significantly improving clinical outcomes and quality of life for patients.

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