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Systematic Journal Review: Recent Developments in The Diagnosis and Therapeutic Management of Sinonasal Carcinoma

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Abstract

Sinonasal carcinoma is a rare aggressive malignancy often detected at an advanced stage due to non-specific initial symptoms. This systematic review aims to summarize recent advances in diagnosis, including imaging technology and biomarkers, and to analyze current therapy management modalities to provide evidence-based recommendations. This study used a Systematic Journal Review (SLR) design following PRISMA guidelines to ensure transparency and accuracy, with a comprehensive literature search from databases such as PubMed and Scopus. Analyzed articles were limited to the last five years (2020-2025) and were narratively synthesized with data extraction covering diagnostic modalities, therapeutic strategies, and clinical outcomes. Trend and density visualization maps revealed a divided research focus: the clinical management cluster (sinonasal cancer, radiotherapy) as the foundation, and the diagnostic cluster (differential diagnosis, SMARCA4-deficient sinonasal ca) as the cutting-edge innovation. Analyzed studies confirmed the importance of genetic biomarkers such as SMARCA4 and HPV status for prognosis and therapy personalization. Overall, the current literature highlights a shift towards multimodal approaches and precision oncology that integrates molecular diagnosis to improve patient outcomes. This review confirms the integration of molecular diagnosis and personalized therapy management as the latest trend in sinonasal carcinoma treatment.

Keywords: *Biomarker, Diagnosis, Human Papillomavirus (HPV), Radiotherapy, Sinonasal Carcinoma.*

Abstrak

Karsinoma sinonasal merupakan tumor ganas langka yang bersifat agresif dan sering terdeteksi pada stadium lanjut akibat gejala awal yang tidak spesifik. Tinjauan sistematis ini bertujuan untuk merangkum perkembangan mutakhir dalam diagnosis, mencakup teknologi pencitraan dan biomarker, serta menganalisis modalitas manajemen terapi terkini untuk memberikan rekomendasi berbasis bukti. Penelitian ini menggunakan desain Systematic Journal Review (SLR) berdasarkan pedoman PRISMA untuk menjamin transparansi dan akurasi, dengan pencarian literatur komprehensif dari basis data seperti PubMed dan Scopus. Artikel yang dianalisis dibatasi pada lima tahun terakhir (2020 2025) dan disintesis secara naratif dengan ekstraksi data mencakup modalitas diagnostik, strategi terapi, dan luaran klinis. Visualisasi peta tren dan kedalaman (density) menunjukkan fokus riset yang terbagi: klaster manajemen klinis (sinonasal cancer, radiotherapy) sebagai fondasi, dan klaster diagnostik (differential diagnosis, SMARCA4-

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deficient sinonasal ca) sebagai inovasi mutakhir. Studi yang dianalisis menegaskan pentingnya biomarker genetik seperti SMARCA4 dan status HPV untuk prognosis dan personalisasi terapi. Secara keseluruhan, literatur terkini menyoroti pergeseran menuju pendekatan multimodal dan precision oncology yang mengintegrasikan diagnosis molekuler untuk meningkatkan outcome pasien. Tinjauan ini menegaskan integrasi diagnosis molekuler dan manajemen terapi personalisasi sebagai tren mutakhir dalam pengelolaan karsinoma sinonasal.

Kata Kunci: Biomarker, Diagnosis, Human Papillomavirus (HPV), Karsinoma Sinonasal, Radiotherapy.

INTRODUCTION

Sinonasal carcinoma represents a relatively rare group of malignant tumors, accounting for less than 1% of all malignancies, yet it is characterized by aggressive biological behavior and high morbidity and mortality (Binazzi et al., 2024; Consonni et al., 2024). Despite its low incidence, the clinical burden of this disease is substantial, primarily due to its anatomical location within the nasal cavity and paranasal sinuses, which are closely associated with critical structures such as the orbit, skull base, and cranial nerves. This complex anatomy not only limits the feasibility of radical surgical resection but also increases the risk of intracranial and orbital invasion, thereby worsening clinical outcomes.

A major clinical challenge in sinonasal carcinoma lies in its early presentation, which is frequently marked by nonspecific symptoms such as nasal obstruction, epistaxis, facial pressure, or rhinorrhea. These manifestations often mimic benign or chronic inflammatory sinonasal conditions, leading to misinterpretation, delayed referral, and postponed diagnostic evaluation (Papadopoulou et al., 2021; Thawani et al., 2023). As a consequence, many patients are diagnosed at an advanced stage, when therapeutic options are more limited and prognosis is significantly poorer (Chmielewski, 2024; Indrasari et al., 2023). This persistent diagnostic delay highlights the urgent need for improved clinical awareness and more effective diagnostic strategies to facilitate earlier detection.

In recent years, significant advances in diagnostic modalities have improved the ability to detect and characterize sinonasal tumors. High-resolution magnetic resonance imaging (MRI) has enhanced soft-tissue contrast and improved the assessment of perineural spread and intracranial extension, while positron emission tomography–computed tomography (PET-CT) has provided valuable metabolic information that increases staging accuracy and supports treatment planning (Awais et al., 2023; El-Adem et al., 2023). Parallel progress in pathology, particularly through immunohistochemistry and molecular profiling using next-generation sequencing (NGS), has refined histopathological classification, revealed tumor heterogeneity, and identified molecular alterations with prognostic and therapeutic relevance (Bhai et al., 2023; Bracigliano et al., 2021; Taverna et al., 2022). These developments underscore the evolving complexity of sinonasal carcinoma diagnosis and management.

Therapeutically, sinonasal carcinoma remains a challenging entity due to its biological heterogeneity and anatomical constraints. Multimodal treatment approaches combining surgery, radiotherapy, and systemic therapy are often required to achieve optimal outcomes. However, survival rates remain suboptimal for several subtypes. For example, a meta-analysis by Mauthe et al., (2023) reported that although combined surgery and radiotherapy were commonly employed in adenoid cystic carcinoma, long-term survival outcomes were still variable, with a 5-year overall survival of approximately 68%. These findings suggest that advances in treatment modalities have not yet fully translated into uniformly improved prognoses.

Although multiple systematic reviews and meta-analyses have examined specific subtypes or isolated aspects of sinonasal carcinoma, the existing literature remains fragmented. Prognostic analyses are frequently conducted separately for individual entities, such as de novo sinonasal squamous cell carcinoma or carcinoma arising from inverted papilloma, without integration across other histological subtypes (Vuong & Nguyen, 2022). Similarly, molecular and biological reviews often focus on genetic or epigenetic mechanisms in isolation, without linking these findings to contemporary clinical outcomes or therapeutic strategies (Lumbanraja et al., 2023). To date, there is no comprehensive synthesis that integrates recent diagnostic advances, molecular insights, and therapeutic outcomes across the full spectrum of sinonasal carcinoma subtypes. This fragmentation constitutes a significant gap in the literature and limits the development of unified, evidence-based clinical guidance.

Therefore, this study aims to systematically identify and synthesize recent developments in the diagnosis and management of sinonasal carcinoma, encompassing advances in imaging, histopathology, biomarkers, and molecular profiling. In addition, it seeks to critically evaluate current therapeutic modalities, including surgery, radiotherapy, chemotherapy, and targeted therapies, based on the latest available evidence. By integrating findings across different subtypes and clinical approaches, this systematic review is expected to provide a comprehensive and up-to-date perspective that supports earlier diagnosis, optimized treatment strategies, and improved clinical outcomes.

The systematic review methodology is particularly suited to addressing this objective, as it enables transparent literature selection, minimizes bias, and facilitates structured evidence synthesis (Page et al., 2021). Through critical appraisal and comparison of existing studies, this approach allows identification of consistent patterns, knowledge gaps, and methodological limitations within the current body of research. Consequently, this study contributes not only to clinical practice but also to future research directions by offering an integrated, evidence-based framework for understanding and managing sinonasal carcinoma.

METHOD

This study employed a Systematic Literature Review (SLR) design to identify, evaluate, and synthesize recent scientific evidence related to developments in the diagnosis and therapeutic management of sinonasal carcinoma. The SLR approach was selected due to its ability to provide a comprehensive, structured, and transparent synthesis of current evidence, particularly in addressing fragmented findings across diverse tumor subtypes and clinical approaches. The review process was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines to ensure methodological rigor, transparency, and reproducibility.

A comprehensive literature search was carried out using multiple electronic databases, including PubMed, Scopus, Web of Science, ScienceDirect, and Google Scholar. The search strategy utilized combinations of the following keywords with Boolean operators AND and OR:

1. “Sinonasal carcinoma” OR “Sinonasal cancer”
2. “Diagnosis” OR “Diagnostic approach”
3. “Management” OR “Treatment”
4. “Therapy” OR “Therapeutic strategy”
5. “Head and neck malignancy”

To ensure relevance to contemporary clinical practice, only articles published between January 2020 and March 2025 were considered eligible for inclusion.

Inclusion and Exclusion Criteria

The inclusion criteria were defined as follows:

1. Original research articles, systematic reviews, or meta-analyses published in peer-reviewed journals between 2020 and 2025.
2. Studies focusing on sinonasal carcinoma, including specific histopathological subtypes (e.g., squamous cell carcinoma, adenoid cystic carcinoma, neuroendocrine carcinoma).
3. Articles reporting on diagnostic modalities (imaging, histopathology, immunohistochemistry, molecular or biomarker-based approaches) and/or therapeutic management (surgery, radiotherapy, chemotherapy, targeted therapy, or multimodal treatment).
4. Studies providing measurable clinical outcomes such as survival rates, local control, recurrence, or treatment-related complications.
5. Articles published in English with accessible full texts.

Exclusion criteria included conference abstracts without full texts, case reports, editorials, letters to the editor, non-peer-reviewed articles, and studies that did not specifically address sinonasal carcinoma or lacked relevance to diagnostic or therapeutic outcomes.

Study Selection and Data Extraction

Two independent reviewers conducted the screening process, beginning with title and abstract evaluation based on the predefined eligibility criteria. Full-text assessments were subsequently performed for potentially relevant articles. Any discrepancies between reviewers were resolved through discussion, and a third reviewer was consulted when consensus could not be reached.

Data were extracted systematically from the included studies, covering:

1. Author(s), publication year, and country of origin
2. Study design and patient population characteristics
3. Diagnostic modalities employed (e.g., CT, MRI, PET-CT, histopathology, immunohistochemistry, molecular analysis)
4. Therapeutic management strategies (endoscopic or open surgery, radiotherapy including IMRT, chemotherapy, targeted therapy, or combined modalities)
5. Reported clinical outcomes (overall survival, disease-free survival, recurrence rates, adverse events, and complications)

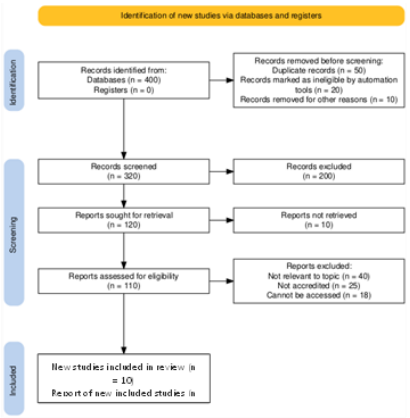

Figure 1. PRISMA Flow Diagram

The study selection process is illustrated using a PRISMA flow diagram. From an initial identification of 400 records, 80 articles were removed prior to screening due to duplication (n = 50), automated exclusion (n = 20), or other reasons (n = 10). A total of 320 articles underwent title and abstract screening, resulting in the exclusion of 200 articles. Subsequently, 120 full-text articles were assessed for eligibility, of which 10 were inaccessible. After further exclusion based on irrelevance, insufficient quality, or incomplete data, 27 studies met all inclusion criteria and were included in the final synthesis. A narrative synthesis approach was employed to summarize and integrate findings across the included studies. The results were supported by tables outlining study characteristics and comparisons among diagnostic and therapeutic modalities. Where applicable, analyses were stratified according to tumor subtype, diagnostic approach, or treatment modality to enhance interpretability and clinical relevance.

Data analysis was performed using thematic coding through the VOSviewer software. Each selected article was reduced into analytical units based on relevant variables and categorized into four major themes: (1) Recent diagnostic approaches for pediatric nasopharyngeal carcinoma, (2) Clinical management, (3) Multimodal therapy, and (4) Multidisciplinary approaches. Coding was conducted iteratively to maintain consistency and objectivity in data interpretation. The results of the coding process were synthesized into a thematic conceptual model that illustrates current clinical practices and future research directions.

RESULT

Article Screening Results

The process of searching and screening journals was conducted using the *Publish or Perish* software, resulting in 10 journals selected based on the highest ranking determined by the greatest number of citations.

Table 1. Article Screening Results Based on PRISMA Criteria According to the Top 10 Most Cited Publications

No	Authors	Year	Title	Journal
1	(Taverna et al., 2022)	2020	*SMARCA4-deficient sinonasal carcinoma: a series of 10 cases expanding the genetic spectrum of SWI/SNF-driven sinonasal malignancies*	*The American Journal of Surgical Pathology*
2	(Thawani et al., 2023)	2023	*The contemporary management of cancers of the sinonasal tract in adults*	*CA: A Cancer Journal for Clinicians*
3	(Paver et al., 2020)	2020	*Human papilloma virus related squamous cell carcinomas of the head and neck: diagnosis, clinical implications and detection of HPV*	*Pathology*
4	(Thompson & Bishop, 2022)	2022	*Update from the 5th Edition of the World Health Organization classification of head and neck tumors: nasal cavity, paranasal sinuses and skull base*	*Head and Neck Pathology*
5	(Williams et al., 2022)	2022	*Molecular detection methods in HPV-related cancers*	*Frontiers in Oncology*

6	(Agaimy et al., 2020)	2020	*Recurrent loss of SMARCA4 in sinonasal teratocarcinosarcoma*	*The American Journal of Surgical Pathology*
7	(Millen et al., 2023)	2023	*Patient-derived head and neck cancer organoids allow treatment stratification and serve as a tool for biomarker validation and identification*	*Medical Journal*
8	(Elgart & Faden, 2020)	2020	*Sinonasal squamous cell carcinoma: etiology, pathogenesis, and the role of human papilloma virus*	*Current Otorhinolaryngology Reports*
9	(Bracigliano et al., 2021)	2021	*Malignant sinonasal tumors: update on histological and clinical management*	*Current Oncology*
10	(Ferrari et al., 2021)	2021	*Sinonasal squamous cell carcinoma, a narrative reappraisal of the current evidence*	*Frontiers in Oncology*

The screening results using PRISMA criteria indicate that the ten articles with the highest citation counts were dominated by topics related to updated classifications, molecular detection, and contemporary management of sinonasal carcinoma. These findings demonstrate that advances in diagnosis are heavily oriented toward biomarkers and genetic mutations such as *SMARCA4*, which has become an important trend in recent literature. In addition, several articles emphasize the significance of multidisciplinary therapeutic approaches, including the use of patient-derived organoids for treatment stratification. The variety of high-impact journals such as *CA: A Cancer Journal for Clinicians*, *The American Journal of Surgical Pathology*, and *Cancers* demonstrates the high quality of the evidence produced. Overall, these findings confirm that research on sinonasal carcinoma continues to develop rapidly, particularly in the areas of precision diagnostics and personalized therapy.

Table 2. Data Extraction of Systematic Journal Review Articles on Recent Advances in Diagnosis and Therapeutic Management of Sinonasal Carcinoma

No	Authors / Year	Study Title	Key Findings
1	Agaimy et al., 2020	*SMARCA4-deficient sinonasal carcinoma: a series of 10 cases expanding the genetic spectrum of SWI/SNF-driven sinonasal malignancies*	Identified *SMARCA4* mutations as a novel genetic factor in sinonasal carcinoma, demonstrating a broader SWI/SNF genetic spectrum and potential molecular therapeutic targets.
2	Thawani et al., 2023	*The contemporary management of cancers of the sinonasal tract in adults*	Reviewed current management strategies, including endoscopic surgery, precision radiotherapy, and combination chemotherapy, with evidence-based treatment recommendations.

3	Paver et al., 2020	*Human papilloma virus related squamous cell carcinomas of the head and neck: diagnosis, clinical implications and detection of HPV*	Emphasized the importance of HPV detection in sinonasal squamous cell carcinoma, which influences prognosis and therapeutic decisions.
4	Thompson & Bishop, 2022	*Update from the 5th Edition of the World Health Organization classification of head and neck tumors: nasal cavity, paranasal sinuses and skull base*	Updated WHO classification for sinonasal tumors, providing more accurate diagnostic and histopathological guidelines.
5	Williams et al., 2022	*Molecular detection methods in HPV-related cancers*	Described modern molecular methods for HPV detection, including PCR and sequencing, improving diagnostic accuracy and therapeutic stratification.
6	Rooper et al., 2020	*Recurrent loss of SMARCA4 in sinonasal teratocarcinosarcoma*	Showed recurrent loss of *SMARCA4* in sinonasal teratocarcinosarcoma, potentially serving as a prognostic biomarker and therapeutic target.
7	Millen et al., 2023	*Patient-derived head and neck cancer organoids allow treatment stratification and serve as a tool for biomarker validation and identification*	Utilized patient-derived organoids for testing therapeutic responses and validating biomarkers, supporting personalized treatment approaches.
8	Elgart & Faden, 2020	*Sinonasal squamous cell carcinoma: etiology, pathogenesis, and the role of human papilloma virus*	Highlighted the etiology and pathogenesis of sinonasal squamous cell carcinoma, as well as the role of HPV in tumor development and therapeutic choices.
9	Bracigliano et al., 2021	*Malignant sinonasal tumors: update on histological and clinical management*	Provided histological and clinical management updates, emphasizing multidisciplinary approaches for optimal therapeutic outcomes.
10	Ferrari et al., 2021	*Sinonasal squamous cell carcinoma, a narrative reappraisal of the current evidence*	Reviewed current evidence on sinonasal squamous cell carcinoma, emphasizing surgery, radiotherapy, and immunotherapy as components of modern treatment standards.

Based on the extraction table above, most articles emphasize the advancement of molecular diagnostics and more accurate histopathological classifications for sinonasal carcinoma. Several studies, such as those by Agaimy et al., (2020) and Rooper et al.,

(2020), reveal the role of *SMARCA4* as a potential genetic biomarker, opening opportunities for the development of molecular targeted therapies. In addition, HPV detection is also a major focus in sinonasal squamous cell carcinoma because it affects prognosis and therapeutic strategies (Elgart & Faden, 2020; Paver et al., 2020). In terms of therapeutic management, recent literature highlights multimodal approaches that combine surgery, radiotherapy, chemotherapy, and targeted therapy or immunotherapy. Ferrari et al., (2021) and Thawani et al., (2023) stress the importance of evidence-based treatment strategies, whereas the use of patient-derived organoids by Millen et al., (2023) reinforces personalized approaches in selecting optimal therapies. A multidisciplinary approach is essential for improving outcomes in patients with sinonasal carcinoma. Overall, this review demonstrates that precision diagnostics and evidence-based and molecular therapy are the latest trends in the management of sinonasal carcinoma. The implementation of molecular technologies, the latest WHO classification, and the identification of specific biomarkers such as *SMARCA4* and HPV status have become primary focuses in enhancing diagnostic accuracy and therapeutic effectiveness. The findings indicate an integration between molecular diagnostics and personalized therapeutic management in sinonasal carcinoma. The identification of genetic biomarkers and viral infections, accurate tumor classification, and the application of multimodal approaches are key strategies to improve patient prognosis and safety. This approach reflects a shift from conventional management toward *precision oncology*, in which therapy is tailored to the molecular and clinical characteristics of each patient, enabling more effective and measurable treatment decisions.

DISCUSSION

The findings of this systematic review demonstrate a clear paradigm shift in the diagnosis and management of sinonasal carcinoma, moving from conventional morphology-based approaches toward an integrated molecular and precision-based framework. Rather than standing as isolated discoveries, advancements in genetic profiling, histopathological classification, and molecular detection technologies collectively reshape how sinonasal tumors are understood, classified, and treated. This evolution reflects a broader transformation in oncology, where tumor behavior is increasingly defined by molecular characteristics rather than anatomical location alone.

One notable convergence in the literature is the growing emphasis on genetic alterations within the SWI/SNF chromatin-remodeling complex, particularly SMARCA4 mutations. While Agaimy et al., (2020) highlight SMARCA4 loss as a defining diagnostic marker associated with aggressive tumor behavior, Rooper et al., (2020) extend this observation by emphasizing its prognostic relevance and therapeutic implications. The difference between these perspectives lies in their clinical orientation: one prioritizes diagnostic stratification, while the other foregrounds treatment planning. Together, these findings suggest that SMARCA4 status functions not merely as a diagnostic label, but as a bridge linking pathology, prognosis, and therapeutic decision-making. This integration underscores the future role of molecular pathology as an active contributor to clinical oncology rather than a passive diagnostic tool.

Parallel to genetic biomarkers, viral oncogenesis particularly Human Papilloma Virus (HPV) infection adds another layer of complexity to sinonasal carcinoma classification. Unlike SMARCA4-driven tumors, HPV-associated sinonasal squamous cell carcinomas often demonstrate a more favorable prognosis. This contrast highlights how distinct etiological pathways can lead to clinically divergent tumor behaviors. Paver et al., (2020) and Williams et al., (2022) illustrate that advancements in molecular detection techniques such as PCR and next-generation sequencing do not merely improve

diagnostic sensitivity, but also enable meaningful clinical stratification. When integrated with genetic data, HPV status helps clinicians tailor treatment intensity, potentially reducing overtreatment and improving patient safety. This convergence of viral and genetic biomarkers illustrates a future diagnostic ecosystem where multiple molecular signals are interpreted collectively rather than independently.

The refinement of diagnostic accuracy is further reinforced by updates to the WHO classification of sinonasal tumors. Thompson & Bishop (2022) emphasize that these revisions are not merely taxonomic but clinically consequential, as they align histological subtypes with emerging molecular insights. When viewed alongside biomarker discoveries, the WHO framework acts as a unifying structure that translates molecular complexity into standardized clinical practice. This integration ensures that advances in laboratory research are systematically incorporated into diagnostic workflows, thereby reducing variability in interpretation and improving interprofessional communication.

In terms of therapeutic management, the literature reflects a transition from uniform treatment protocols toward biologically informed multimodal strategies. Thawani et al., (2023) describe how endoscopic surgery, precision radiotherapy, and combination chemotherapy are increasingly deployed in a complementary manner. However, the novelty lies not in the modalities themselves, but in how they are selected and combined based on tumor biology. For example, tumors characterized by aggressive genetic profiles may warrant intensified systemic therapy, whereas HPV-positive tumors may benefit from treatment de-escalation strategies. This adaptive approach illustrates how molecular diagnostics directly influence therapeutic architecture.

Emerging technologies such as patient-derived organoids further strengthen this personalized paradigm. Unlike traditional predictive models, organoids allow clinicians to simulate therapeutic responses prior to clinical intervention (Millen et al., 2023). When integrated with genetic and histopathological data, organoids function as translational tools that connect laboratory findings with real-world clinical decisions. This approach not only enhances therapeutic precision but also minimizes trial-and-error treatment, aligning closely with the goals of precision oncology.

Finally, the increasing complexity of diagnostic and therapeutic decision-making underscores the necessity of multidisciplinary collaboration. Bracigliano et al., (2021) and Ferrari et al., (2021) emphasize that optimal outcomes in sinonasal carcinoma depend on coordinated efforts among pathologists, oncologists, radiologists, and surgeons. As molecular data, imaging technologies, and biological models become more sophisticated, interdisciplinary integration becomes essential to ensure that innovations translate into tangible clinical benefits.

In summary, the collective evidence from this systematic review indicates that the future of sinonasal carcinoma management lies in the integration of molecular biomarkers, advanced diagnostic technologies, and personalized therapeutic strategies. Rather than representing isolated advancements, genetic profiling, viral detection, updated classification systems, and organoid-based testing together form a cohesive framework for precision oncology. This transformation holds significant promise for improving diagnostic accuracy, optimizing treatment selection, and ultimately enhancing patient outcomes and safety.

CONCLUSION

Based on the research conducted, it can be concluded that this systematic review successfully synthesizes current evidence regarding the effectiveness of Proton Pump Inhibitors (PPIs) in the management of Laryngopharyngeal Reflux Disease (LPRD), although the reported findings demonstrate considerable variation. Several prospective

studies, particularly those from India, consistently report significant improvements in the Reflux Symptom Index (RSI) and Reflux Finding Score (RFS) following PPI therapy. However, these findings are contrasted by a meta-analysis from China, which shows no statistically significant difference between PPI and placebo in the overall improvement of LPRD symptoms. This substantial discrepancy highlights the complex and highly heterogeneous nature of LPRD, wherein symptoms tend to be nonspecific and diagnosis heavily relies on clinical indices. In addition to effectiveness, this review also emphasizes the long-term risks associated with PPI usage, such as the potential increased risk of gastric cancer, and introduces a newer therapeutic alternative, potassium-competitive acid blockers (PCABs), for refractory LPRD cases.

Although the widespread use of PPIs and their clinical benefits in managing LPRD have been well established, this review highlights notable limitations in the existing literature, particularly the lack of direct investigation into biomarkers. There remains a research gap concerning the measurement of specific biochemical biomarkers, such as Glutathione S-transferase (GST) and Interleukin-1 beta (IL-1β), in clinical studies of LPRD. This gap indicates the need for a deeper understanding of the pathophysiology of LPRD and more individualized treatment approaches. Therefore, clinicians are encouraged to adopt a more personalized approach in managing LPRD, given that acid suppression alone does not always yield optimal outcomes for all patients. Lifestyle modifications and consideration of alternative therapies also represent important components of management, particularly when PPIs are ineffective or when long-term use raises safety concerns.

Future research should prioritize the integration of specific biochemical biomarkers, such as GST and IL-1β, into clinical studies to predict and monitor patient responses to PPI therapy in LPRD. Investigation of these biomarkers has the potential to offer important insights into the inflammatory pathways underlying the disease, which may explain the variability in PPI effectiveness among patient populations. Furthermore, studies should focus on establishing standardized diagnostic criteria for LPRD by combining clinical indices with objective biomarker measurements to achieve more accurate patient stratification. Long-term prospective studies are also needed to evaluate the sustained effectiveness of PPIs and the impact of personalized treatment approaches based on biomarker profiles. A multifaceted approach that integrates clinical evaluation with biomarker analysis is essential for optimizing therapeutic outcomes in LPRD.

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