International Journal of Innovative Technologies in Social Science

e-ISSN: 2544-9435

Scholarly Publisher
RS Global Sp. z O.O.
ISNI: 0000 0004 8495 2390

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ARTICLE TITLE	GASTRIC MALT LYMPHOMA – CURRENT DIAGNOSTIC AND THERAPEUTIC STRATEGIES
DOI	https://doi.org/10.31435/ijitss.4(48).2025.4226
RECEIVED	31 October 2025
ACCEPTED	26 December 2025
PUBLISHED	30 December 2025
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GASTRIC MALT LYMPHOMA – CURRENT DIAGNOSTIC AND THERAPEUTIC STRATEGIES

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ABSTRACT

Gastric mucosa-associated lymphoid tissue (MALT) lymphoma is a distinct subtype of extranodal marginal zone B-cell lymphoma strongly associated with Helicobacter pylori infection. This review presents an overview of current diagnostic and therapeutic strategies, highlighting recent developments in molecular diagnostics and evidence-based management. The diagnosis relies on histopathological evaluation supported by immunohistochemistry and molecular testing for characteristic translocations, particularly t(11;18)(q21;q21). First-line therapy remains H. pylori eradication, which induces complete and durable remission in most patients, including some who are H. pylori-negative. For those unresponsive to antibiotics, radiotherapy or rituximab-based immunotherapy achieves excellent local control and survival rates. Prognosis is generally favourable, with five-year overall survival exceeding 90%. However, complications such as gastrointestinal bleeding, perforation, and histologic transformation into diffuse large B-cell lymphoma (DLBCL) may occur. Early detection, accurate staging, and an individualized, risk-adapted therapeutic approach remain key factors influencing long-term outcomes. Advances in endoscopic imaging, molecular characterization, and targeted therapies continue to refine the management of gastric MALT lymphoma, supporting the trend toward more personalized treatment strategies and improved patient prognosis.

KEYWORDS

Gastric MALT Lymphoma, Helicobacter Pylori Eradication, Endoscopic Diagnosis, Radiotherapy, Immunochemotherapy

CITATION

Jonatan Rataj, Kamil Harenza, Karolina Ollik, Marlena Radzka, Michalina Kosowska, Justyna Jankowska, Adrianna Wiekiera, Mateusz Wiekiera. (2025). Gastric MALT Lymphoma – Current Diagnostic and Therapeutic Strategies. *International Journal of Innovative Technologies in Social Science*. 4(48). doi: 10.31435/ijitss.4(48).2025.4226

Introduction

Gastric mucosa-associated lymphoid tissue (MALT) lymphoma represents the most common form of extranodal marginal zone B-cell lymphoma (P. G. Isaacson & Du, 2004; Zucca et al., 2013). Although Helicobacter pylori eradication can induce remission in many cases, variations in molecular background and treatment response continue to pose clinical challenges (Zucca et al., 2020). Recent advances in diagnostic techniques and therapeutic strategies have refined disease management and highlighted the importance of individualized approaches (Nakamura & Hojo, 2022; Raderer & Kiesewetter, 2021). This review aims to summarize current knowledge on diagnostic and therapeutic strategies in gastric MALT lymphoma, emphasizing evolving perspectives in clinical practice.

Methods

This systematic review evaluates strategies of diagnostic and treatment of gastric MALT lymphoma. A comprehensive literature search was conducted across PubMed and Google Scholar. Eligible publications comprised randomized controlled trials, prospective and retrospective cohort studies, meta-analyses, and systematic reviews. The methodological quality of each study was rigorously appraised to ensure validity and minimize bias in the synthesis of evidence.

Definition and Epidemiology

It is widely recognized that primary gastric lymphoma (PGL) is defined as the most common form of extranodal non-Hodgkin lymphoma, accounting for approximately 30–40% of all such cases. Within the spectrum of gastrointestinal lymphomas, the stomach represents the most frequently involved organ, followed by the small intestine and colon (Nakamura & Matsumoto, 2013). Previous studies have consistently reported that the incidence of PGL is two to three times higher in males than in females. Among the histological subtypes, mucosa-associated lymphoid tissue (MALT) lymphoma constitutes the predominant variant

(Cogliatti et al., 1991; Shimm et al., 1983). MALT lymphoma is characterized as a low-grade non-Hodgkin lymphoma composed of small- to medium-sized neoplastic B cells, primarily of marginal zone type, with occasional immunoblasts (Bayerdörffer et al., 1997; Nakamura et al., 1995; Wotherspoon et al., 1991) This entity was first described by Isaacson and Wright in 1984 (P. Isaacson & Wright, 1984; Nakamura & Hojo, 2022). It should be noted that any part of the stomach may be affected, although the antrum is most frequently involved, accounting for approximately 40% of cases (Violeta Filip et al., 2018; Zullo et al., 2010). The disease most commonly occurs between the ages of 50 and 60; however, a notable trend has been observed toward increasing incidence among individuals over 40 years of age (Juárez-Salcedo et al., 2018). Gastric MALT lymphoma is generally regarded as a relatively rare malignancy, with an estimated incidence ranging between 0.3 and 0.8 cases per 100,000 individuals in Europe (Ullrich et al., 2002).

Pathophysiology and mechanisms

It is generally accepted that gastric MALT lymphoma is a type of lymphoma that can be categorised as a low-grade neoplasm. The disease is characterised by a dense lymphoid infiltration that leads to the invasion and subsequent destruction of gastric glands. This process ultimately results in the formation of what is known as a "lymphoepithelial lesion," which is widely regarded as a hallmark feature of lymphoma diagnosis (Violeta Filip et al., 2018). It has been well established that gastric MALT lymphomas are strongly associated with *Helicobacter pylori* infection (Wang et al., 2014). Epidemiological studies have estimated that between 80 and 90 per cent of patients diagnosed with gastric MALT lymphoma are infected with *H. pylori* (Nakamura & Hojo, 2022). In *H. pylori*-dependent cases, the growth of lymphoma cells appears to be driven by immune responses generated by *H. pylori* that include signalling from CD40 and CD86 with the help of bystander T cells(Nakamura & Hojo, 2022). Furthermore, it has been demonstrated that APRIL (a proliferation-inducing ligand), which is produced by eosinophils in *H. pylori*-infected gastric mucosa, plays a crucial role in promoting the survival and proliferation of neoplastic B cells (Blosse et al., 2020). However, recent studies have reported that the incidence of *H. pylori*-negative gastric MALT lymphoma is increasing, accounting for approximately 10–30% of all cases (Kiesewetter et al., 2021). Genetic predisposition has been identified as a significant factor in the pathogenesis of gastric MALT lymphoma. Previous research has demonstrated a high prevalence of specific human leukocyte antigen (HLA) alleles, notably HLA-DQA10103 and HLA-DQB10601, among affected individuals (Kawahara et al., 2005). Additionally, the R702W mutation in the NOD2/CARD15 gene has frequently been observed, suggesting that it may contribute to disease susceptibility and immune dysregulation within the gastric mucosa (Rosenstiel et al., 2006). A growing body of evidence indicates that chromosomal translocations in MALT lymphomas, such as t(11;18)(q21;q21), t(1;14)(p22;q32), t(14;18)(q32;q21), and t(3;14)(p14.1;q32), play an important role in lymphomagenesis, either through chimeric protein formation (e.g., BIRC3-MALT1) or transcriptional deregulation of BCL10, MALT1, and FOXP1. Taken together, these genetic alterations converge on the NF-κB signaling pathway, highlighting its central role in MALT lymphoma pathogenesis (Du, 2016; Streubel et al., 2004). In immunohistochemistry, MALT lymphoma cells typically express CD20+, CD79a+, and BCL2+, while lacking BCL6, CD5, CD10, and CD23 expression (Ishikawa et al., 2022).

Diagnosis

It is important to note that the clinical manifestations of gastric MALT lymphoma tend to be non-specific, most commonly presenting with symptoms such as dyspepsia and abdominal pain. In the majority of reported cases, these complaints are mild and often attributed to benign gastric disorders. However, as the disease progresses, more severe manifestations have been observed, including vomiting, chronic gastric bleeding, iron-deficiency anaemia, and weight loss (Violeta Filip et al., 2018; Zullo et al., 2010).

Although uncommon, it has been documented that some patients may exhibit classic B symptoms—such as fever and night sweats—which are typically regarded as characteristic features of B-cell lymphomas. In rare instances, the disease may progress to cause gastric wall perforation, particularly when associated with extensive lymphoid infiltration (El Asmar et al., 2016).

Esophagogastroduodenoscopy

In clinical practice, it is generally accepted that endoscopy represents the first and most essential step in diagnosing gastric MALT lymphoma, apart from conducting a thorough patient interview. However, it should be emphasized that endoscopic findings are often inconclusive. The endoscopic appearance of the disease has been shown to be highly variable, as it can closely resemble benign conditions—such as erosions or multifocal gastritis—or mimic malignant lesions such as gastric adenocarcinoma (Inagaki et al., 2004).

Endoscopic manifestations of gastric MALT lymphoma can be broadly categorized into four main morphological patterns: superficial lesions (41%), mass-forming types (43%), diffuse infiltrative changes (6%), and other or unclassified appearances (10%) (Nakamura et al., 1995).

Moreover, magnified endoscopic imaging has revealed that a characteristic tree-like appearance (TLA) and ballooning (swelling of surface ducts) are frequently observed, typically accompanied by amorphous, whitish areas(Nakamura & Hojo, 2022; Watanabe et al., 2024).

Histological biopsy

Histological biopsy is widely regarded as the gold standard for the diagnosis of gastric MALT lymphoma (Violeta Filip et al., 2018).

As previously reported in the literature, given the potential for multifocal tumor distribution and the possible coexistence of high-grade components in gastric MALT lymphoma (Psyrri et al., 2008), it has been recommended that multiple endoscopic biopsies be obtained not only from macroscopically abnormal mucosa but also from areas that appear normal under endoscopic examination.

This recommendation is particularly relevant in view of the fact that gastric MALT lymphoma originates in the deep mucosa or submucosa and may progress without disrupting the foveolar glandular architecture, which constitutes the superficial mucosal layer. Consequently, there is a risk that false-negative biopsy results may occur, especially when sampling is confined to visibly abnormal lesions (Park & Lee, 2019).

To ensure greater diagnostic accuracy and to minimise sampling error, biopsies should therefore be systematically obtained from both abnormal and normal-appearing mucosa, including the antrum, the greater and lesser curvatures of the gastric body, and the fundus, with at least two representative tissue samples collected from each anatomical region (Hu et al., 2016).

The definitive diagnosis of gastric MALT lymphoma is established in accordance with histopathological criteria outlined in the World Health Organization (WHO) classification system, and follows the recommendations of the European Gastro-Intestinal Lymphoma Study Group (EGILS) consensus report and the clinical guidelines of the National Comprehensive Cancer Network (NCCN) (Nakamura & Hojo, 2022).

Histologically, gastric MALT lymphomas are characterised by a diffuse infiltrate of atypical neoplastic lymphoid cells (centrocyte-like cells) around reactive follicles, typically exhibiting a marginal zone growth pattern. These cells frequently infiltrate the gastric glands, causing eosinophilic change and destruction of epithelial cells, known as lymphoepithelial lesions (LELs) (Ruskoné-Fourmestraux et al., 2011).

According to established diagnostic practice, a confident diagnosis of gastric MALT lymphoma can therefore be achieved by applying the Wotherspoon scoring system.

Gastric MALT lymphoma has been shown to exhibit a strong association with *Helicobacter pylori* infection; therefore, assessment of *H. pylori* status is essential and should incorporate multiple complementary techniques, including rapid urease testing, histological evaluation, culture, urea breath testing, or stool antigen testing (Fischbach & Malfertheiner, 2018; Malfertheiner et al., 2017). Given that hematoxylin and eosin staining demonstrates limited sensitivity for *H. pylori* detection and a reduced capacity to identify non-spiral or coccoid bacterial forms, it is often necessary to employ special stains—such as Giemsa, Warthin–Starry, or Alcian blue—or immunohistochemical staining, which provides the highest degree of sensitivity and specificity (Hartman & Owens, 2012). It is widely accepted that the presence of *H. pylori* has a pivotal impact on overall prognosis in patients with gastric MALT lymphoma.

Table 1. Wotherspoon score - Histologic scoring system for the diagnosis of gastric MALT lymphoma (Wotherspoon et al., 1993).

Score	Definition	Histologic features
0	Normal	Scattered plasma cells in lamina propria. No lymphoid follicles.
1	Chronic active gastritis	Small clusters of lymphocytes in mucosa. No lymphoid follicles. No lymphoepithelial lesions.
2	Chronic active gastritis with florid lymphoid follicle formation	Prominent lymphoid follicles with surrounding mantle zone and plasma cells. No lymphoepithelial lesions.
3	Suspicious lymphoid infiltrate in mucosa, probably reactive	Lymphoid follicles surrounded by small lymphocytes that infiltrate diffusely in lamina propria and occasionally into epithelium.
4	Suspicious lymphoid infiltrate in mucosa, probably lymphoma	Lymphoid follicles surrounded by marginal zone cells that infiltrate diffusely in lamina propria and into epithelium in small groups.
5	MALT lymphoma	Dense diffuse lamina propria infiltrate of marginal zone cells with prominent lymphoepithelial lesions.

The neoplastic lymphocytes infiltrating the glands are immunophenotypically characterised as atypical B-cells, which can be identified through immunohistochemical staining for B-cell and epithelial markers such as CD20+, CD79a+, CD5-, CD10-, CD23-, CD43+/-, and cyclin D1- (Hu et al., 2016; Nakamura & Matsumoto, 2013; Ruskoné-Fourmestraux et al., 2011).

When large neoplastic cells are observed forming confluent sheets, the diagnosis should be revised to an associated diffuse large B-cell lymphoma (DLBCL) (Ruskoné-Fourmestraux et al., 2011).

The identification of immunoglobulin light chain (κ or λ) restriction by immunohistochemistry or *in situ* hybridisation, in combination with analyses for the clonality of rearranged immunoglobulin genes by polymerase chain reaction (PCR), has been shown to facilitate the diagnosis of B-cell lymphoma (Hu et al., 2016).

In diagnostically ambiguous cases, it has been suggested that molecular testing may be valuable not only for confirming the diagnosis but also for providing additional prognostic insight. The most frequent genetic alteration identified in gastric MALT lymphoma is known to be the t(11;18)(q21;q21) translocation, which results in the API2–MALT1 fusion gene. This abnormality occurs in approximately 25% of cases and is generally associated with a poor response to therapy (Du & Atherton, 2006). Detection of this translocation can be reliably achieved using *in situ* fluorescence hybridisation (FISH) or reverse transcriptase–polymerase chain reaction (RT-PCR).

Notably, patients negative for the t(11;18)(q21;q21) translocation have demonstrated a higher therapeutic response rate and longer median survival than those positive for the translocation (78% vs. 22%). In light of these findings, it is therefore recommended that FISH for t(11;18)(q21;q21) be performed as a routine diagnostic test on formalin-fixed tissue sections in newly diagnosed patients (Park & Lee, 2019).

Other translocations, such as t(3;14)(p14;q32)/FOXP1–IGH, t(1;14)(p22;q32)/BCL10–IGH, and t(14;18)(q32;q21)/IGH–MALT1, have been reported only rarely, and their precise clinical significance remains to be fully elucidated (Bacon et al., 2007).

Staging in Gastric MALT Lymphoma

Accurate staging of gastric MALT lymphoma is widely recognised as essential for optimal clinical management, since tumor depth, nodal involvement, and dissemination patterns have been shown to exert a significant influence on prognosis and therapeutic decision-making (Violeta Filip et al., 2018)

Among the various staging systems proposed, the modified Ann Arbor classification (Musshoff) remains the most commonly employed framework for staging gastric lymphomas. In this system:

- IE – disease confined to the stomach without lymph node involvement:
- IE1 – limited to the mucosa and submucosa
- IE2 – invasion into the muscularis propria or beyond
- IIE – involvement of lymph nodes:
- IIE1 – involvement of perigastric nodes
- IIE2 – involvement of subdiaphragmatic nodes
- IIIE – involvement of the gastrointestinal tract and/or lymph nodes on both sides of the diaphragm
- IVE – dissemination beyond the gastrointestinal tract to other tissues or organs (Violeta Filip et al., 2018)

In addition to the Musshoff system, the Paris (TNMB) classification, proposed by the European Gastro-Intestinal Lymphoma Study Group (EGILS), offers a more detailed and anatomically precise description of tumor involvement. Specifically, it categorises disease according to:

- T – depth of invasion into the gastrointestinal wall,
- N – nodal involvement (regional vs. distant),
- M – distant metastases,
- B – bone marrow involvement

(Ruskoné-Fourmestraux et al., 2011). Taken together, these complementary systems provide a comprehensive framework for evaluating disease extent and guiding evidence-based therapeutic strategies.

Treatment and Management

H. pylori eradication therapy is widely regarded as the first-line treatment for gastric MALT lymphoma, irrespective of the patient's *H. pylori* infection status or disease stage. This therapeutic approach is strongly endorsed by the majority of European clinical guidelines (Dreyling et al., 2013; Ruskone-Fourmestr... et al., 2001). Numerous studies have demonstrated that antibiotic therapy aimed at eradicating *Helicobacter pylori* results in regression and durable remission of gastric MALT lymphoma in approximately 80% of affected patients. In keeping with these findings, antibiotic therapy is also recommended as the initial management strategy for gastric MALT lymphoma in patients who test negative for *H. pylori* (Nakamura et al., 2012; Ono et al., 2010; Ruskone-Fourmestr... et al., 2001; Stathis et al., 2009; Takigawa et al., 2021). Although it might be assumed that the absence of infection would limit therapeutic efficacy, a growing body of evidence suggests that a subset of *H. pylori*-negative patients still experience tumor regression following eradication therapy. For instance, Raderer et al. (Raderer et al., 2006, 2015) reported an excellent response rate of 83% in *H. pylori*-negative gastric MALT lymphoma, whereas earlier investigations indicated conflicting outcomes, with no significant response to antibiotics in this subgroup (Steinbach et al., 1999; Ye et al., 2003). This discrepancy highlights an ongoing controversy, and according to the most recently published NCCN guidelines, *H. pylori*-negative patients should be managed primarily with radiotherapy, or—where contraindicated—with immunotherapy using rituximab (*Guidelines Detail*, n.d.). In terms of treatment regimen, standard triple therapy—comprising a proton-pump inhibitor administered for four weeks in combination with clarithromycin and either amoxicillin or metronidazole for 14 days—has consistently shown high efficacy. The only exception is Pylera®, a bismuth-based quadruple formulation combining bismuth subcitrate, metronidazole, and tetracycline, administered together with omeprazole for 10 days (Ishikawa et al., 2022; Matysiak-Budnik et al., 2023). Following successful eradication, most patients with minimal histological residual gastric MALT lymphoma achieve complete remission after a latency period exceeding 12 months. According to the GELA criteria, complete regression of lymphoma is defined as the absence of lymphoid infiltrate or the presence of minimal residual aggregates (pMRD), provided that macroscopic lesions have resolved. Partial histological response (rRD) or no change (NC) indicates non-regression, although an adequate observation period must be allowed before confirming this outcome to avoid unnecessary interventions [W Fischbach 2022]. Therefore, in line with current expert consensus, most clinical guidelines recommend an observation period of up to 24 months before initiating alternative therapeutic interventions. Nevertheless, there is evidence to suggest that in a subset of patients, delayed lymphoma regression may occur even beyond this timeframe, with late

responses documented over several subsequent years (Matysiak-Budnik et al., 2019; Nakamura et al., 2012; Ruskone-Fourmestr... et al., 2001). Several studies have further evaluated the so-called "watch-and-wait" approach in patients with persistent residual disease after *H. pylori* eradication, demonstrating that it may yield favourable long-term outcomes and carries a relatively low risk of progression to high-grade lymphoma (Choi et al., 2013; Moleiro et al., 2016).

Other therapies

Non-response to *Helicobacter pylori* eradication therapy has been reported in approximately 17–61% of patients with gastric MALT lymphoma. A considerable number of studies have confirmed that radiotherapy, immunotherapy, and chemotherapy represent effective second-line therapeutic options for these patients (Choi et al., 2013; Gong et al., 2016; Ishioka et al., 2021; Stathis et al., 2009). Radiotherapy (RT) is widely recognised as a well-established second-line treatment for localized gastric MALT lymphoma unresponsive to *H. pylori* eradication. Evidence suggests that moderate-dose RT achieves excellent long-term outcomes, with a 10-year recurrence-free rate of 92% in one cohort and a 95% complete remission rate in a larger study using a median dose of 30 Gy, while maintaining minimal toxicity (Goda et al., 2010; Yahalom et al., 2021). Furthermore, it has been demonstrated that reduced doses (e.g., 25.2 Gy) are equally effective, and that field reduction from extended-field RT (EFRT) to involved-field RT (IFRT) has led to improved tolerability and clinical outcomes (Reinartz et al., 2019).

Although RT remains highly effective for localized gastrointestinal lymphomas, its applicability to the small intestine is somewhat limited due to anatomical mobility (Akasaka et al., 2012; Okamura et al., 2012). Nevertheless, stage-adapted RT has consistently demonstrated strong local control and survival benefits. Recent developments have introduced innovative strategies such as involved-site RT (ISRT) and very-low-dose RT (4 Gy), which appear to offer promising therapeutic alternatives associated with reduced toxicity and shorter treatment duration, as supported by ongoing clinical trials (Imber et al., 2021). With regard to systemic therapy, chemotherapy and rituximab-based immunotherapy have been shown to be effective treatment modalities for gastric MALT lymphoma. These approaches are particularly indicated in patients presenting with advanced-stage disease, evidence of dissemination, or histologic transformation to diffuse large B-cell lymphoma (DLBCL) (Fischbach, 2014; Levitt et al., 2009). While the R-CHOP regimen (rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisolone) is considered relatively intensive and potentially toxic for indolent MALT lymphoma, alternative regimens such as R-COP—which omits doxorubicin—have demonstrated favourable tolerability profiles and sustained efficacy (Alderuccio et al., 2022; Morigi et al., 2020; Sugizaki et al., 2018). A pivotal Phase III trial demonstrated that the combination of rituximab and chlorambucil produced superior response rates compared to chlorambucil monotherapy, highlighting the therapeutic advantage of combined regimens (Zucca et al., 2013). More recently, it has been reported that rituximab combined with bendamustine can induce complete remission after as few as three treatment cycles, underscoring its efficacy in selected cases (Salar et al., 2017). Notably, observational studies indicate that patients who received *H. pylori* eradication followed by additional therapy achieved slightly higher five-year overall survival rates compared to those managed exclusively with non-eradication strategies (84.3% vs. 78.5%) Matysiak-Budnik et al. 2019). Taken together, these findings support the view that a tailored, stage-adapted therapeutic approach yields optimal outcomes in gastric MALT lymphoma. Surgery currently is not regarded as a valid treatment option.

Prognosis and Recurrence

Gastric MALT lymphoma generally follows an indolent clinical course and is associated with favourable long-term outcomes (Kim et al., 2021; Sim et al., 2024; Zullo et al., 2010).

As previously demonstrated in large cohort studies, a Japanese multicentre investigation involving 323 patients with gastric MALT lymphoma (GML) confirmed the durability of remission following *Helicobacter pylori* eradication therapy. Using stringent GELA criteria over a median follow-up period of six years (range: 3–14.6 years), complete remission was achieved in 77% of patients, with a remarkably low relapse rate of only 3.1%. Among 97 non-responders, 27 developed progressive disease requiring further treatment, whereas 14 of the remaining 70 were successfully managed through a conservative watch-and-wait approach (Nakamura et al., 2012).

Overall survival (OS) outcomes across different populations have consistently been excellent, with 5-year OS rates frequently exceeding 90%, while lymphoma-specific mortality remains below 5%. Transformation to high-grade lymphoma appears to be uncommon. Nevertheless, despite the high rate of

complete remission, late recurrence may still occur several years after histological clearance, underscoring the need for prolonged endoscopic and histological surveillance.

Consistent prognostic indicators identified across studies include older age and higher clinical stage (II or above), whereas factors such as *H. pylori* status, endoscopic appearance, and tumour location generally do not predict relapse (Qi et al., 2022; Sim et al., 2024).

Although infrequent, bacterial reinfection following eradication therapy has been documented, which further reinforces the necessity of structured, long-term follow-up to enable early detection of either reinfection or lymphoma recurrence (Zullo et al., 2010).

Importantly, the majority of relapse cases respond favourably to second-line therapy, including radiotherapy or other localised interventions, and patients tend to maintain excellent overall survival when closely monitored.These findings highlight the importance of careful risk stratification, taking into account variables such as age, stage, and histopathological features, to inform the development of individualised surveillance protocols and tailored management strategies. Such an approach is particularly valuable for patients who are *H. pylori*-negative or present with advanced-stage disease (Kim et al., 2021; Qi et al., 2022; Sim et al., 2024; Zullo et al., 2010).

Complications

Gastric MALT lymphoma only rarely gives rise to serious clinical complications, although such events can significantly influence both management strategies and overall prognosis. Among these complications, one of the most critical is massive upper gastrointestinal (GI) bleeding, which may result in hemodynamic instability. It is well established that peptic ulcers represent the predominant cause of upper GI bleeding (≈59%), whereas malignancies, including gastric MALT lymphoma, account for only a small proportion of cases—approximately 2–4%. Bleeding as an initial manifestation of MALT lymphoma has been reported in approximately 15.6% of patients and tends to occur infrequently in early-stage disease (Bestari et al., 2019; Rahman et al., 2022).

Perforation represents another uncommon yet clinically severe complication of gastric MALT lymphoma, which may arise either from direct tumor invasion or as an adverse effect of chemotherapy. Although *H. pylori* eradication remains the initial therapeutic approach in most cases, antibiotic resistance or disease progression may necessitate chemotherapy, which in turn can predispose to treatment-related perforations, sometimes occurring within the first few weeks of therapy. This complication carries considerable morbidity and mortality risks, including generalized peritonitis, sepsis, multi-organ failure, delayed chemotherapy, prolonged hospitalization, and increased mortality, and typically requires prompt surgical intervention (Zayati et al. 2023;).

Although *H. pylori* eradication therapy is generally regarded as both safe and effective, it may fail in patients harbouring specific genetic alterations such as the MALT1 translocation or trisomy 18q21. In such cases, gastric MALT lymphoma can progress independently of *H. pylori*, occasionally evolving into an aggressive phenotype such as diffuse large B-cell lymphoma (DLBCL). This histologic transformation constitutes a major clinical concern, as it is associated with poorer prognosis and necessitates systemic chemotherapy to achieve complete remission (Saito et al., 2024). Additional predictors of non-response to eradication therapy have also been identified, including the presence of chromosomal translocation t(11;18)/API2–MALT1, which leads to dysregulation of MALT1 or BCL10 (Liu et al., 2001; 2002). This translocation has been reported in approximately 7–25% of gastric MALT lymphoma cases and is frequently associated with strong nuclear BCL10 expression (Matysiak-Budnik et al., 2023; Nakamura et al., 2012).

Taken together, these findings underscore the fact that such complications can profoundly influence clinical decision-making and patient outcomes, thereby highlighting the importance of early diagnosis, careful risk stratification, and timely therapeutic intervention.

Conclusions

Gastric MALT lymphoma is a largely curable malignancy when managed according to established diagnostic and therapeutic algorithms. The strong link with *H. pylori* infection underlines the value of eradication therapy as the first-line treatment, while radiotherapy and immunotherapy provide effective second-line options. With early diagnosis and appropriate risk stratification, long-term prognosis remains excellent. The development of dedicated clinical guidelines and advances in endoscopic imaging and molecular diagnostics are expected to further improve in vivo diagnosis and optimize therapeutic strategies.

Author's Contribution

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All authors have read and agreed with the published version of the manuscript.

Funding Statement: This research received no external funding.

Conflict of Interest Statement: The authors declare no conflict of interest.

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