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Diagnostic Gaps in the Endoscopic Recognition of Autoimmune Atrophic Gastritis

დიაგნოსტიკური ხარვეზები აუტოიმუნური ატროფიული გასტრიტის ენდოსკოპიურ ამოცნობაში

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Abstract

Introduction: Autoimmune atrophic gastritis (AAG) is a chronic immune-mediated gastric disorder characterized by corpus-predominant oxyntic atrophy, parietal cell loss, hypochlorhydria, and impaired absorption of iron and vitamin B12. Although upper gastrointestinal endoscopy is routinely performed in clinical practice, AAG is frequently recognized late, often after hematological, neurological, or neoplastic complications have already developed. This structured narrative review examines why endoscopic recognition of AAG continues to lag behind histological diagnosis. **Methods:** Evidence from clinical studies, systematic reviews, meta-analyses, and international guidelines was synthesized to identify disease-related, endoscopist-related, procedure-related, and guideline-related contributors to missed diagnosis. **Results:** The review shows that early AAG may produce subtle or nonspecific mucosal changes, while advanced disease may overlap endoscopically with *Helicobacter pylori*-associated atrophic gastritis. Limited endoscopist awareness, inadequate inspection, non-systematic biopsy strategies, interobserver variability, and inconsistent guideline recommendations further contribute to delayed recognition. Image-enhanced endoscopy and artificial intelligence-assisted systems offer promising opportunities to improve mucosal assessment and reduce diagnostic variability, but they should be regarded as adjuncts to careful inspection, clinical suspicion, and systematic biopsy protocols. **Conclusions**: The findings suggest that AAG should be understood not only as an autoimmune gastric disease but also as a quality-of-endoscopy challenge. Earlier recognition requires targeted endoscopic training, standardized reporting, risk-based mapping biopsies, clearer guideline integration, and validation of emerging technologies in real-world clinical settings.

Keywords: Autoimmune atrophic gastritis; autoimmune gastritis; endoscopy; diagnostic delay; gastric atrophy; biopsy protocol; image-enhanced endoscopy; artificial intelligence; gastric neuroendocrine tumor; gastric precancerous conditions.

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აბსტრაქტი

შესავალი: აუტოიმუნური ატროფიული გასტრიტი წარმოადგენს ქრონიკულ იმუნომედიირებულ კუჭის დაავადებას, რომელიც ხასიათდება კორპუსის უპირატესი ოქსინტური ატროფიით, პარიეტული უჯრედების დაზიანებით, ჰიპოქლორჰიდრიით და რკინისა და ვიტამინ B12-ის შეწოვის დარღვევით. მიუხედავად იმისა, რომ ზედა გასტროინტესტინური ენდოსკოპია კლინიკურ პრაქტიკაში ფართოდ გამოიყენება, აუტოიმუნური ატროფიული გასტრიტი ხშირად გვიან დიაგნოსტირდება, როდესაც ჰემატოლოგიური, ნევროლოგიური ან ნეოპლაზიური გართულებები უკვე განვითარებულია. მოცემული სტრუქტურირებული ნარატიული მიმოხილვის მიზანია ახსნას, რატომ ჩამორჩება დაავადების ენდოსკოპიური ამოცნობა ჰისტოლოგიურ დიაგნოზს. **მეთოდოლოგია:** კლინიკური კვლევების, სისტემური მიმოხილვების, მეტაანალიზებისა და საერთაშორისო გაიდლაინების მონაცემების სინთეზის საფუძველზე გაანალიზდა დიაგნოსტიკური ხარვეზების დაავადებასთან, ენდოსკოპისტთან, პროცედურასთან და გაიდლაინებთან დაკავშირებული ფაქტორები. **შედეგები:** კვლევა აჩვენებს, რომ ადრეულ სტადიაზე დაავადება შესაძლოა გამოვლინდეს შეუმჩნეველი ან არასპეციფიკური ლორწოვანი ცვლილებებით, ხოლო პროგრესირებულ ეტაპზე ენდოსკოპიურად დაემსგავსოს *Helicobacter pylori*-თან ასოცირებულ ატროფიულ გასტრიტს. დიაგნოსტიკურ დაგვიანებას ასევე ხელს უწყობს ენდოსკოპისტების არასაკმარისი ცნობიერება, არასისტემური ბიოფსიის სტრატეგია, ინტერპრეტაციის ცვალებადობა და გაიდლაინების არათანმიმდევრულობა. გამოსახულებით გაძლიერებული ენდოსკოპია და ხელოვნური ინტელექტის სისტემები პერსპექტიული დამხმარე ინსტრუმენტებია, თუმცა ისინი ვერ ანაცვლებენ კლინიკურ ეჭვს, ხარისხიან დათვალიერებასა და სისტემურ ბიოფსიას. აუტოიმუნური ატროფიული გასტრიტი უნდა განვიხილოთ არა მხოლოდ როგორც აუტოიმუნური კუჭის დაავადება, არამედ როგორც ენდოსკოპიის ხარისხის პრობლემა. **დასკვნა:** ადრეული ამოცნობის გაუმჯობესება მოითხოვს მიზნობრივ სწავლებას, სტანდარტიზებულ ანგარიშგებას, რისკზე დაფუძნებულ ბიოფსიის პროტოკოლს, გაიდლაინების უკეთ ინტეგრაციას და ახალი ტექნოლოგიების რეალურ კლინიკურ გარემოში ვალიდაციას.

საკვანძო სიტყვები: აუტოიმუნური ატროფიული გასტრიტი; აუტოიმუნური გასტრიტი; ენდოსკოპია; დიაგნოსტიკური დაგვიანება; კუჭის ატროფია; ბიოფსიის პროტოკოლი; გამოსახულებით გაძლიერებული ენდოსკოპია; ხელოვნური ინტელექტი; კუჭის ნეიროენდოკრინული სიმსივნე; კუჭის პრეკანცერული მდგომარეობები.

რეკომენდირებული ციტირება: ომარ ბაკურაძე, ქეთევან ომიაძე. დიაგნოსტიკური ხარვეზები აუტოიმუნური ატროფიული გასტრიტის ენდოსკოპიურ ამოცნობაში. *ჯანდაცვის პოლიტიკა, ეკონომიკა და სოციოლოგია,* 10 (2). DOI: https://doi.org/10.52340/healthecosoc.2026.10.02.9

Introduction

Autoimmune atrophic gastritis (AAG) is a chronic immune-mediated disorder characterized by progressive destruction of parietal cells in the gastric corpus and fundus. This process is driven primarily by autoreactive CD4+ T lymphocytes and circulating autoantibodies against parietal cell and intrinsic factor antigens, leading to corpus-predominant oxyntic atrophy, hypochlorhydria or achlorhydria, and impaired absorption of iron and vitamin B12 (Castellana et al., 2024; Lenti et al., 2020). Although AAG may remain clinically silent for many years, its consequences are clinically significant. Iron deficiency may precede pernicious anemia, while vitamin B12 deficiency can lead to hematological and neurological complications, some of which may become irreversible if diagnosis is delayed (Lenti et al., 2020). In

addition, AAG is recognized as a premalignant condition associated with an increased risk of type I gastric neuroendocrine tumors and, more controversially, gastric adenocarcinoma (Angerilli et al., 2024; Chen et al., 2023).

Despite its clinical importance, AAG remains under-recognized in routine gastroenterological practice. Earlier estimates suggested a prevalence of approximately 0.1%–2% in the general population, with higher rates among women and older adults (Rustgi et al., 2021). However, more recent evidence indicates that the true burden may be substantially higher than previously assumed, partly because diagnostic criteria and case-finding strategies differ across studies and clinical settings (Li et al., 2025). The problem is not merely epidemiological. AAG often presents with nonspecific gastrointestinal symptoms, unexplained iron deficiency, vitamin B12 deficiency, or associated autoimmune diseases, and many patients remain asymptomatic until advanced atrophic changes or complications have already developed (Carabotti et al., 2017; Chen et al., 2025; Kalkan & Soykan, 2016). This delayed recognition limits opportunities for timely surveillance, risk stratification, and prevention of neoplastic progression.

Upper gastrointestinal endoscopy occupies a central position in the diagnosis and management of AAG. Histopathological confirmation of corpus-predominant atrophy requires endoscopic biopsy, and endoscopic surveillance is essential for detecting gastric neuroendocrine tumors, dysplasia, and early malignancy (Dinis-Ribeiro et al., 2025; Shah et al., 2021). However, the relationship between endoscopy and diagnosis is paradoxical. Although endoscopy provides access to the mucosa and enables biopsy, AAG is frequently missed during the endoscopic encounter. Histological diagnosis may reveal AAG only after biopsies are taken for other reasons, while the visual endoscopic diagnosis may lag behind or remain absent. Lenti et al. (2019) reported a median diagnostic delay of 14 months, highlighting that the disease is often identified only after prolonged clinical uncertainty. This suggests that AAG should not be viewed solely as a rare or clinically silent condition, but also as a problem of endoscopic recognition and quality.

Several factors contribute to this diagnostic gap. First, early AAG may produce only subtle mucosal changes, such as mild pallor, vascular visibility, or minimal corpus-predominant atrophy, which can be difficult to distinguish from normal variation or other forms of chronic gastritis (Kamada et al., 2023; Kishino & Nonaka, 2022). Second, AAG may overlap endoscopically with Helicobacter pylori-associated atrophic gastritis, particularly when both conditions coexist or when prior H. pylori eradication changes the distribution of atrophy (Dottori et al., 2024; Nishizawa et al., 2021). Third, diagnostic accuracy depends heavily on endoscopist awareness, inspection quality, use of image-enhanced endoscopy, and adherence to systematic biopsy protocols such as the updated Sydney System (Dinis-Ribeiro et al., 2025; Shah et al., 2021). Fourth, substantial interobserver variability in the endoscopic grading of gastric atrophy limits reproducibility and may contribute to inconsistent recognition across clinical settings (Kawamura et al., 2015).

International guidelines also differ in the extent to which they support endoscopic recognition of AAG. The American Gastroenterological Association emphasizes histological confirmation and topographic biopsies in the diagnosis and management of atrophic gastritis (Shah et al., 2021). The European MAPS III guideline focuses on staging, surveillance, and the use of virtual chromoendoscopy for gastric precancerous conditions (Dinis-Ribeiro et al., 2025). Japanese guidance provides more detailed descriptions of endoscopic features of autoimmune gastritis, including attention to early-stage disease (Kamada et al., 2023). These differences indicate that current guidance is not fully harmonized, particularly regarding how endoscopists should suspect AAG before histological confirmation. As a result, the probability of recognition may depend not only on disease severity but also on the endoscopist's training, local protocols, and the guideline framework being followed.

Recent advances in image-enhanced endoscopy and artificial intelligence may help address this gap. Narrow-band imaging and magnifying endoscopy can improve visualization of mucosal and vascular patterns associated with gastric atrophy and intestinal metaplasia, although evidence specifically focused on AAG remains limited (Rokkas & Ekmektzoglou, 2023; Yagi et al., 2012). Artificial intelligence systems

have shown promising diagnostic performance for chronic atrophic gastritis and are now being developed specifically for autoimmune gastritis, with the potential to support non-expert endoscopists and reduce interobserver variability (Chen et al., 2024; Shi et al., 2023). Nevertheless, these technologies cannot substitute for appropriate clinical suspicion, systematic inspection, and correct biopsy strategy.

The existing literature has addressed the epidemiology, pathophysiology, clinical presentation, and neoplastic risks of AAG, as well as the general role of endoscopy in gastric precancerous conditions. However, fewer studies have integrated these issues into a focused explanation of why endoscopic recognition of AAG fails and how this failure may be corrected. This review addresses that gap by examining AAG as a quality-of-endoscopy problem. Its objective is to analyze the disease-related, endoscopist-related, and procedure-related factors that contribute to missed endoscopic diagnosis; to clarify the clinical consequences of delayed recognition; and to evaluate current and emerging strategies for improving detection. The guiding research questions are: (1) What role does endoscopy play in the diagnostic delay of AAG? (2) Why is AAG missed endoscopically despite subsequent histological confirmation? (3) What are the clinical consequences of delayed recognition? and (4) Can image-enhanced endoscopy and artificial intelligence reduce missed diagnoses?

Methods

This study was designed as a structured narrative review aimed at examining diagnostic gaps in the endoscopic recognition of autoimmune atrophic gastritis (AAG). A narrative review approach was selected because the objective was not to estimate a pooled diagnostic effect size, but to integrate evidence from clinical studies, systematic reviews, meta-analyses, expert reviews, and international guidelines in order to explain why AAG remains under-recognized during routine upper gastrointestinal endoscopy. Particular attention was given to disease-related, endoscopist-related, procedure-related, and guideline-related factors that may contribute to delayed or missed diagnosis.

A structured literature search was conducted in PubMed, Scopus, and Google Scholar for publications issued between 2009 and 2026. The search combined Medical Subject Headings (MeSH) and free-text terms related to autoimmune gastritis, atrophic gastritis, endoscopic diagnosis, gastric precancerous conditions, biopsy protocols, image-enhanced endoscopy, and artificial intelligence. The main search terms included “autoimmune atrophic gastritis,” “autoimmune gastritis,” “atrophic gastritis,” “corpus-predominant atrophy,” “endoscopy,” “endoscopic diagnosis,” “diagnostic delay,” “diagnostic accuracy,” “gastric atrophy,” “Helicobacter pylori gastritis,” “biopsy protocol,” “updated Sydney System,” “OLGA,” “OLGIM,” “narrow-band imaging,” “image-enhanced endoscopy,” “magnifying endoscopy,” “artificial intelligence,” “gastric neuroendocrine tumor,” and “gastric cancer.” Boolean operators were used to combine terms and refine search results.

Studies were considered eligible if they addressed at least one of the following topics: the epidemiology or clinical presentation of AAG; diagnostic delay or under-recognition of AAG; endoscopic features of autoimmune gastritis; differentiation between AAG and *Helicobacter pylori*-associated atrophic gastritis; biopsy strategies for gastric atrophy; interobserver variability in endoscopic assessment; endoscopic surveillance of premalignant gastric conditions; or the role of image-enhanced endoscopy and artificial intelligence in detecting gastric atrophy or autoimmune gastritis. Priority was given to systematic reviews, meta-analyses, guideline documents, multicenter studies, large cohort studies, and clinically relevant expert reviews. Case reports were used only when they illustrated a specific diagnostic challenge or unresolved clinical issue. Publications that did not focus on gastric atrophy, autoimmune gastritis, endoscopic diagnosis, or premalignant gastric conditions were excluded.

In addition to peer-reviewed articles, major international guidelines and consensus documents were reviewed and compared. These included the American Gastroenterological Association Clinical Practice Update on atrophic gastritis, the European MAPS III guideline on epithelial precancerous conditions and lesions in the stomach, the Japanese Gastroenterological Endoscopy Society framework

on endoscopic features of autoimmune gastritis, and the National Institute for Health and Care Excellence guideline on vitamin B12 deficiency (Dinis-Ribeiro et al., 2025; Kamada et al., 2023; National Institute for Health and Care Excellence, 2024; Shah et al., 2021). These documents were analyzed with regard to four domains: the assigned role of endoscopy, the presence or absence of AAG-specific endoscopic criteria, biopsy recommendations, and surveillance guidance.

Data were synthesized thematically rather than statistically. The analysis was organized around four core questions: (1) how endoscopy contributes to or mitigates diagnostic delay in AAG; (2) why AAG may be missed during endoscopic examination despite later histological confirmation; (3) what clinical consequences follow from delayed endoscopic recognition; and (4) whether current or emerging technologies, including image-enhanced endoscopy and artificial intelligence, can reduce missed diagnoses. Evidence was grouped into disease-related factors, including subtle early mucosal changes and overlap with *H. pylori*-associated gastritis; endoscopist-related factors, including awareness and recognition skills; procedure-related factors, including inspection quality and biopsy strategy; and system-level factors, including differences between international guidelines.

Because this study is a narrative review rather than a systematic review, it did not include formal risk-of-bias assessment, quantitative meta-analysis, or protocol registration. This design allows broad integration of clinical and guideline-based evidence, but it also introduces potential limitations, including publication bias, selective availability of data, and interpretive subjectivity. To reduce these limitations, the review prioritized recent high-quality sources, compared evidence across different clinical settings and guideline traditions, and distinguished between established findings and areas where evidence remains limited or controversial.

Literature Review

Epidemiology and Clinical Significance of Autoimmune Atrophic Gastritis

Chronic atrophic gastritis may develop through different etiological pathways, most commonly as a consequence of long-standing *Helicobacter pylori* infection or as a result of autoimmune destruction of the oxyntic mucosa. Autoimmune atrophic gastritis (AAG), historically referred to as type A gastritis, is distinguished by corpus-predominant atrophy, relative antral sparing, parietal cell loss, and autoimmune serological markers (Lenti et al., 2020). In contrast, *H. pylori*-associated atrophic gastritis usually begins in the antrum and may progress proximally over time. This distinction is clinically important because the two conditions may overlap endoscopically, coexist in the same patient, or be confused during routine examination (Kamada et al., 2023; Nishizawa et al., 2021).

The true prevalence of AAG remains difficult to establish. Earlier studies estimated its prevalence at approximately 0.1%–2% in the general population, increasing among women and older adults (Rustgi et al., 2021). More recent evidence suggests that these figures may underestimate the real disease burden. A systematic review and meta-analysis reported a higher pooled global prevalence, indicating that AAG may be more common than previously recognized (Li et al., 2025). This variation reflects differences in diagnostic definitions, study populations, biopsy practices, use of serological markers, and clinical awareness. Since many patients are diagnosed only after anemia, neurological symptoms, or neoplastic complications emerge, prevalence estimates based only on clinically recognized disease are likely to miss a substantial number of undiagnosed cases.

AAG has a marked demographic pattern. It is more frequently reported in older adults and shows a female predominance, with studies indicating higher rates among women, particularly in association with other autoimmune conditions (Lahner et al., 2022; Rustgi et al., 2021). However, the perception that AAG is restricted mainly to elderly women or to Northern European populations may itself contribute to diagnostic bias. Recent data from Asian and American populations suggest that AAG may be under-recognized outside traditionally described high-risk groups (Chen et al., 2025; Rustgi et al., 2021).

Therefore, clinicians should avoid interpreting AAG as a narrowly defined demographic disease and should instead consider it in patients with compatible endoscopic, hematological, autoimmune, or histological findings.

Pathophysiology of Autoimmune Atrophic Gastritis

The pathogenesis of AAG is based on immune-mediated destruction of gastric parietal cells. Autoreactive CD4+ T lymphocytes target the gastric H+/K+-ATPase proton pump in the corpus and fundus, leading to progressive loss of oxyntic glands (Lenti et al., 2020). B-cell activation contributes to the production of anti-parietal cell antibodies and anti-intrinsic factor antibodies, which are important diagnostic markers but are not sufficient as stand-alone diagnostic tests because of limitations in sensitivity and specificity (Castellana et al., 2024; Conti et al., 2020).

Parietal cell loss produces two major physiological consequences. First, reduced gastric acid secretion impairs the conversion of dietary ferric iron into the absorbable ferrous form, contributing to iron deficiency. This may occur years before vitamin B12 deficiency becomes clinically evident (Hershko & Camaschella, 2014; Lenti et al., 2020). Second, intrinsic factor deficiency reduces vitamin B12 absorption in the terminal ileum, eventually leading to pernicious anemia and neurological complications. In advanced cases, vitamin B12 deficiency may cause peripheral neuropathy, cognitive symptoms, gait disturbance, and subacute combined degeneration of the spinal cord, some of which may not fully reverse after delayed treatment (Lenti et al., 2020).

Another key consequence of parietal cell loss is hypergastrinemia. As gastric acidity declines, feedback inhibition of antral G cells is reduced, resulting in chronically elevated gastrin levels. Persistent hypergastrinemia stimulates enterochromaffin-like cell hyperplasia and may lead to the development of type I gastric neuroendocrine tumors (Castellana et al., 2024; Lenti et al., 2020). This mechanism explains why AAG is not only a disorder of malabsorption but also a premalignant gastric condition requiring endoscopic recognition and surveillance.

Clinical Manifestations and Diagnostic Delay

AAG typically has an insidious onset and may remain asymptomatic for years. In many patients, the disease is not suspected until unexplained iron deficiency anemia, vitamin B12 deficiency, dyspeptic symptoms, or autoimmune comorbidity prompts further investigation. A large retrospective cohort found that a substantial proportion of patients were asymptomatic at diagnosis, while many others presented with nonspecific complaints rather than classic pernicious anemia (Chen et al., 2025). This clinical variability contributes to delayed referral for endoscopy and delayed histological confirmation.

When symptoms are present, they are often nonspecific. Patients may report dyspepsia, postprandial discomfort, abdominal pain, bloating, nausea, reflux-like symptoms, fatigue, or signs of anemia (Carabotti et al., 2017; Soykan et al., 2025). The presence of reflux-like symptoms is diagnostically important because AAG is characterized by reduced acid secretion, yet some patients still report heartburn or regurgitation. This paradox may lead to treatment with proton pump inhibitors without adequate investigation of the underlying gastric mucosal pathology (Tenca et al., 2016). As a result, the diagnosis may be postponed until more advanced atrophic changes or complications develop.

The hematological manifestations of AAG also have diagnostic implications. Iron deficiency may be the earliest clinical clue, especially in younger patients and women, whereas vitamin B12 deficiency and pernicious anemia may appear later in the disease course (Lenti et al., 2020). Failure to respond adequately to oral iron or vitamin B12 supplementation should raise suspicion of an underlying malabsorptive condition, including AAG (Castellana et al., 2024). However, if clinicians rely only on confirmed vitamin B12 deficiency as the entry point for further investigation, earlier stages of AAG may be missed.

AAG is also strongly associated with other autoimmune diseases. Autoimmune thyroid disease is the most frequently reported comorbidity, and the coexistence of autoimmune thyroiditis and autoimmune gastritis is often described as thyrogastric syndrome (Cellini et al., 2017). Increased prevalence has also been reported among patients with type 1 diabetes mellitus, celiac disease, rheumatoid arthritis, and other autoimmune disorders (De Block et al., 2008; Kalkan & Soykan, 2016). Therefore, the presence of autoimmune comorbidity should increase clinical suspicion, particularly when accompanied by anemia, dyspeptic symptoms, or corpus-predominant atrophic changes.

Oncological Risk and the Importance of Endoscopic Recognition

The oncological significance of AAG is one of the strongest arguments for improving endoscopic recognition. AAG is associated with an increased risk of type I gastric neuroendocrine tumors due to chronic hypergastrinemia and enterochromaffin-like cell hyperplasia (Angerilli et al., 2024; Lenti et al., 2020). Although type I gastric neuroendocrine tumors are often indolent, they require detection, classification, surveillance, and, in selected cases, endoscopic or surgical treatment. Missed diagnosis of AAG may therefore delay identification of neuroendocrine lesions and deprive patients of appropriate surveillance.

The relationship between AAG and gastric adenocarcinoma is more complex and remains debated. Some studies report increased gastric cancer risk among patients with autoimmune gastritis, while others argue that the risk may be partly explained by current or previous *H. pylori* infection, intestinal metaplasia, or mixed etiological pathways (Chen et al., 2023; Rugge et al., 2022). Regardless of this controversy, AAG is widely recognized as a condition that may coexist with premalignant gastric changes and therefore requires careful histological staging and endoscopic follow-up when advanced atrophy or intestinal metaplasia is present (Dinis-Ribeiro et al., 2025; Shah et al., 2021).

Endoscopy is central to this process for two reasons. First, histological confirmation of AAG depends on adequate topographic biopsies from the antrum, incisura, and corpus. Without biopsy, serology alone cannot reliably establish the diagnosis or stage the extent of mucosal damage. Second, endoscopy provides the platform for detecting neuroendocrine tumors, dysplasia, and early gastric cancer. Therefore, missed endoscopic recognition is not simply a diagnostic inconvenience; it has direct implications for cancer prevention, surveillance planning, and long-term patient outcomes.

Taken together, the literature indicates that AAG should be understood as a clinically important but frequently under-recognized premalignant condition. Its delayed diagnosis results from a combination of silent progression, nonspecific symptoms, overlap with other gastric disorders, inconsistent biopsy practices, and limited endoscopic awareness. These features make AAG a particularly suitable model for examining how quality of endoscopy, rather than disease biology alone, shapes diagnostic outcomes.

Endoscopic Features and Current Diagnostic Standards

Histological Confirmation and the Role of Endoscopy

The diagnosis of autoimmune atrophic gastritis (AAG) requires integration of clinical, serological, endoscopic, and histopathological findings. Although serological markers such as anti-parietal cell antibodies, anti-intrinsic factor antibodies, hypergastrinemia, and a reduced pepsinogen I/II ratio may support clinical suspicion, histopathological confirmation remains central to diagnosis (Castellana et al., 2024; Lenti et al., 2020). This makes upper gastrointestinal endoscopy indispensable, because it provides both direct mucosal assessment and access to topographic biopsies from the stomach.

The histological hallmark of AAG is corpus-predominant oxyntic atrophy, usually with relative sparing of the antrum. This distribution distinguishes AAG from the more common pattern of *Helicobacter pylori*-associated atrophic gastritis, which typically begins in the antrum and may later extend proximally (Kamada et al., 2023). However, this distinction is not always straightforward. Previous

H. pylori infection, partial regression of antral atrophy after eradication, mixed etiologies, and advanced pangastritis may blur the topographic pattern and complicate endoscopic interpretation (Dottori et al., 2024; Nishizawa et al., 2021).

Because visual assessment alone is insufficient, biopsy strategy is a critical component of diagnosis. The updated Sydney System recommends systematic sampling from five gastric sites: two biopsies from the antrum, one from the incisura angularis, and two from the corpus, ideally placed in separately labeled containers to allow accurate topographic interpretation (Shah et al., 2021). In suspected AAG, careful separation of antral and corpus biopsies is particularly important because the diagnosis depends on recognizing the distribution of atrophy. Inadequate or non-topographic biopsy sampling may result in missed diagnosis, misclassification of disease extent, or failure to distinguish autoimmune from *H. pylori*-associated atrophic gastritis.

Conventional Endoscopic Features of Autoimmune Atrophic Gastritis

In established AAG, conventional white-light endoscopy may reveal characteristic features. The most important pattern is corpus-predominant atrophy with relative antral preservation, often described as a "reverse atrophy" pattern because it contrasts with the antrum-predominant distribution commonly associated with *H. pylori* gastritis (Kamada et al., 2023). Advanced disease may show pale and thinned mucosa, loss of rugal folds, increased visibility of submucosal vessels, and poor distensibility of the gastric body. These features reflect progressive oxyntic gland loss and mucosal thinning.

Another reported finding is adherent mucus in the fundus or upper corpus, which may be seen in some patients with AAG. Magnifying endoscopy may demonstrate closely arranged small round or oval pits in the atrophic corpus, a pattern that differs from some descriptions of *H. pylori*-associated mucosal change (Yagi et al., 2012). However, these findings are not universally present, and their recognition depends on endoscopist experience, image quality, mucosal preparation, and the stage of disease.

Early-stage AAG is more difficult to recognize. At this stage, mucosal changes may be subtle or absent on white-light endoscopy, while histological damage may already be present (Kishino & Nonaka, 2022). Mild pallor, slight vascular visibility, or limited corpus-predominant change may be interpreted as nonspecific gastritis or even normal mucosa. This explains why a normal or near-normal endoscopic impression does not exclude AAG, especially in patients with compatible serology, unexplained iron deficiency, vitamin B12 deficiency, autoimmune comorbidity, or persistent dyspeptic symptoms.

Differentiation from *Helicobacter pylori*-Associated Atrophic Gastritis

Differentiating AAG from *H. pylori*-associated atrophic gastritis is one of the most important diagnostic challenges in routine endoscopy. The two conditions have different pathogenic mechanisms, but their endoscopic appearances may overlap considerably, particularly in advanced atrophic disease. Both may present with mucosal pallor, visible vessels, loss of folds, intestinal metaplasia, and atrophic borders. Therefore, reliance on white-light endoscopic appearance alone may lead to misclassification.

The distinction is further complicated by the fact that AAG and *H. pylori* infection may coexist or occur sequentially. In some patients, prior *H. pylori* infection may produce atrophic changes that persist after eradication. In others, antral atrophy may regress after eradication, leaving a residual corpus-predominant pattern that resembles AAG (Dottori et al., 2024). Nishizawa et al. (2021) showed that autoimmune gastritis may be more difficult to detect after successful *H. pylori* eradication, supporting the need for systematic biopsy protocols in patients with suspicious mucosal patterns or unexplained clinical findings.

This overlap has practical implications. If AAG is mistaken for *H. pylori*-associated gastritis, the autoimmune basis of the disease may remain unrecognized, and patients may not receive appropriate evaluation for iron deficiency, vitamin B12 deficiency, hypergastrinemia, autoimmune comorbidity, or

type I gastric neuroendocrine tumors. Conversely, if *H. pylori*-associated atrophy is misclassified as AAG, patients may undergo inappropriate surveillance or incomplete etiological assessment. Accurate diagnosis therefore requires a combined approach that includes endoscopic pattern recognition, biopsy mapping, histology, *H. pylori* testing, and autoimmune serology.

Staging of Gastric Atrophy and Premalignant Risk

Endoscopic and histological staging systems are used to assess the extent and severity of gastric atrophy and to guide surveillance decisions. The Kimura–Takemoto classification is an endoscopic system that categorizes gastric atrophy according to the location and extension of the atrophic border. Closed-type atrophy is limited mainly to the lesser curvature, whereas open-type atrophy extends more widely across the gastric body. Extensive open-type atrophy is associated with higher gastric cancer risk and often corresponds to more advanced histological stages (Kawamura et al., 2015; Shah et al., 2021).

Histological staging is commonly performed using the Operative Link on Gastritis Assessment (OLGA) and Operative Link on Gastric Intestinal Metaplasia Assessment (OLGIM) systems. These systems classify patients into stages 0–IV according to the severity and topographic extent of atrophy or intestinal metaplasia. Advanced stages, particularly OLGA or OLGIM III–IV, identify patients at increased risk for gastric neoplasia and are used to guide surveillance intervals (Dinis-Ribeiro et al., 2025; Shah et al., 2021). Although these staging systems are not specific for autoimmune etiology, they are clinically useful because they quantify the extent of premalignant gastric change.

For AAG, staging has particular value because the disease may be missed if the endoscopist focuses only on focal lesions rather than the background mucosal pattern. Systematic staging helps shift attention from isolated visible abnormalities to the broader topography of mucosal atrophy. This is especially important because AAG-related neoplastic risk is linked not only to discrete lesions but also to the biological consequences of diffuse oxyntic atrophy, including chronic hypergastrinemia and enterochromaffin-like cell hyperplasia.

Guideline-Based Diagnostic Standards

International guidelines agree that histology is essential for confirming atrophic gastritis, but they differ in how explicitly they address AAG-specific endoscopic recognition. The American Gastroenterological Association emphasizes histological confirmation, topographic biopsies, and clinical risk stratification in the diagnosis and management of atrophic gastritis (Shah et al., 2021). This framework is useful for standardizing biopsy practice but provides limited disease-specific visual criteria for AAG.

The European MAPS III guideline focuses on the diagnosis, staging, and surveillance of gastric precancerous conditions and lesions. It recommends high-quality endoscopy, virtual chromoendoscopy, and histological staging to guide surveillance, particularly in patients with extensive atrophy or intestinal metaplasia (Dinis-Ribeiro et al., 2025). However, it treats atrophic gastritis largely through a cancer-prevention framework and does not provide detailed AAG-specific criteria for early visual recognition.

Japanese endoscopic literature gives greater attention to the specific endoscopic appearance of autoimmune gastritis, including the reverse atrophy pattern and early-stage diagnostic challenges (Kamada et al., 2023; Kishino & Nonaka, 2022). This is important because AAG-specific pattern recognition may help endoscopists suspect the disease before histology is available. In contrast, guidelines focused primarily on vitamin B12 deficiency may assign endoscopy a more reactive role, recommending investigation after clinical or laboratory abnormalities have already emerged (National Institute for Health and Care Excellence, 2024). Such an approach may miss earlier stages of AAG, particularly in patients who present with iron deficiency, dyspepsia, autoimmune comorbidity, or subtle endoscopic changes before overt vitamin B12 deficiency.

Taken together, current diagnostic standards show a structural tension. Histology remains the diagnostic anchor, but histology depends on endoscopic biopsy, and biopsy depends on clinical suspicion, endoscopic recognition, or adherence to mapping protocols. When endoscopists fail to suspect AAG, biopsies may not be taken or may not be taken from the correct sites. Therefore, improving AAG diagnosis requires not only better histopathological interpretation but also better endoscopic awareness, standardized biopsy practice, and clearer guideline integration.

Diagnostic Gaps in Endoscopic Recognition

Although autoimmune atrophic gastritis (AAG) has recognizable clinical, histological, and endoscopic characteristics, it is frequently missed during routine upper gastrointestinal endoscopy. This diagnostic gap does not result from a single cause. Rather, it reflects the interaction of disease-related factors, endoscopist-related factors, procedure-related limitations, biopsy practices, and inconsistencies between international guidelines. Understanding these factors is essential because missed endoscopic recognition delays histological confirmation, risk stratification, and surveillance for gastric neuroendocrine tumors and other premalignant or malignant lesions.

Disease-Related Factors: Subtle Early Mucosal Changes

One of the main reasons AAG is missed endoscopically is that early disease may be visually subtle. In established cases, AAG may show corpus-predominant atrophy, mucosal pallor, visible vessels, loss of rugal folds, and relative antral sparing. However, these features are not always present in early-stage disease. Histological changes may precede obvious endoscopic abnormalities, meaning that the mucosa may appear normal or only minimally altered under white-light endoscopy (Kamada et al., 2023; Kishino & Nonaka, 2022). Mild pallor, slight vascular visibility, or limited corpus change can easily be interpreted as nonspecific gastritis or normal variation.

This creates a diagnostic paradox. AAG requires histological confirmation, but biopsies are often taken only when the endoscopist sees an abnormality or when there is a strong clinical indication. If early mucosal changes are subtle and clinical suspicion is low, systematic biopsies may not be performed. Consequently, the diagnosis may be delayed until more advanced atrophy, anemia, vitamin B12 deficiency, neuroendocrine lesions, or other complications become apparent. In this sense, the silent progression of AAG directly contributes to its under-recognition.

*Overlap With *Helicobacter pylori*-Associated Gastritis*

A second major diagnostic challenge is the endoscopic overlap between AAG and *Helicobacter pylori*-associated atrophic gastritis. Although the two conditions have distinct etiologies, their visual appearances may converge as atrophy progresses. Both may show mucosal thinning, pallor, visible submucosal vessels, loss of folds, and intestinal metaplasia. The typical “reverse atrophy” pattern of AAG, characterized by corpus-predominant atrophy with relative antral sparing, can be difficult to distinguish from post-eradication or advanced *H. pylori*-related changes (Kamada et al., 2023; Nishizawa et al., 2021).

The problem is particularly relevant after *H. pylori* eradication. Regression of antral inflammation or atrophy may leave residual corpus-predominant changes, which can mimic AAG. Dottori et al. (2024) showed that antral atrophy may regress after eradication, altering the topographic pattern and complicating endoscopic interpretation. Conversely, patients with AAG may be incorrectly treated as having persistent or recurrent *H. pylori*-associated gastritis, especially if the autoimmune basis of the disease is not considered. This may lead to repeated eradication attempts, incomplete etiological assessment, and delayed recognition of associated risks such as hypergastrinemia, pernicious anemia, and type I gastric neuroendocrine tumors.

Because of this overlap, endoscopic appearance alone is insufficient. Accurate differentiation requires integration of topographic biopsy findings, *H. pylori* testing, serological markers, gastrin levels, pepsinogen status, and clinical context. Failure to combine these elements is one of the central reasons AAG remains underdiagnosed.

Endoscopist-Related Factors: Limited Awareness and Recognition Skills

Endoscopist awareness plays a crucial role in the recognition of AAG. In routine practice, chronic gastritis is often associated primarily with *H. pylori*, reflux disease, peptic ulcer disease, or nonspecific inflammation. AAG may still be perceived as an uncommon condition mainly linked to pernicious anemia, rather than as a premalignant disorder that can present with iron deficiency, dyspepsia, autoimmune comorbidity, or subtle endoscopic changes (Lenti et al., 2020; Rustgi et al., 2021). This narrow clinical perception may reduce diagnostic suspicion during endoscopy.

Limited awareness is especially problematic because AAG recognition depends on pattern recognition. The endoscopist must notice the distribution of atrophy, compare the corpus and antrum, assess the presence of rugal fold loss, identify vascular visibility, and consider whether the pattern fits autoimmune rather than *H. pylori*-associated disease. Without specific training, these findings may be overlooked or described nonspecifically as “gastritis” or “atrophic changes,” without triggering appropriate biopsies or follow-up.

Evidence from related areas suggests that recognition can improve with structured training. Studies on endoscopic assessment of gastritis and gastric atrophy show that diagnostic agreement and recognition improve after targeted educational interventions (Eshmuratov et al., 2019; Zhao et al., 2020). Although direct studies measuring endoscopist knowledge of AAG remain limited, the available evidence supports the view that missed recognition is partly modifiable. This makes AAG not only a diagnostic problem, but also a training and quality-improvement issue.

Procedure-Related Factors: Inspection Quality and Biopsy Strategy

Procedure quality is another important contributor to missed diagnosis. High-quality upper gastrointestinal endoscopy requires adequate mucosal cleansing, sufficient insufflation, careful inspection time, complete visualization of the stomach, and appropriate photographic documentation. These elements are particularly important in AAG because the disease may present as diffuse background mucosal change rather than as a focal lesion. If inspection is rapid, visualization is poor, or the endoscopist focuses mainly on ulcers, masses, or erosions, corpus-predominant atrophy may be missed.

Biopsy strategy is especially important. Reliance only on targeted biopsies from visually abnormal areas can miss AAG, particularly when mucosal changes are subtle or patchy. The updated Sydney System reduces this risk by recommending systematic biopsies from the antrum, incisura, and corpus, with topographic separation of specimens (Shah et al., 2021). This approach allows the pathologist to determine whether atrophy is corpus-predominant, antrum-predominant, multifocal, or extensive. In suspected AAG, separate labeling of corpus and antral biopsies is essential because the diagnosis depends on the distribution of atrophy.

Inadequate biopsy practice may lead to several errors. If biopsies are not taken, histological diagnosis is impossible. If biopsies are taken only from the antrum, corpus-predominant disease may be missed. If specimens from different sites are placed in the same container, the topographic pattern may be lost. If the biopsy report describes atrophy without site-specific interpretation, the autoimmune pattern may remain unrecognized. Thus, the diagnostic gap is not only visual but also procedural.

Interobserver Variability in Endoscopic Assessment

Interobserver variability is a further barrier to reliable endoscopic recognition of AAG. Even when atrophic changes are present, endoscopists may differ in how they identify, grade, and describe

them. The Kimura–Takemoto classification provides a useful endoscopic framework for grading gastric atrophy, but agreement between observers is imperfect. Kawamura et al. (2015) reported only moderate interobserver agreement in the assessment of gastric mucosal atrophy, even among experienced endoscopists. This variability is likely to be greater in settings where endoscopists have less exposure to AAG or less training in gastric atrophy classification.

Interobserver variability has direct clinical consequences. One endoscopist may identify corpus-predominant atrophy and recommend mapping biopsies, while another may describe the same mucosa as nonspecific gastritis. Such inconsistency can determine whether a patient receives histological confirmation, serological evaluation, and surveillance. Variability also complicates guideline implementation, because surveillance recommendations depend on the extent and severity of atrophy. When endoscopic grading is inconsistent, risk stratification becomes less reliable.

Structured image-based training, standardized reporting terminology, and use of image-enhanced endoscopy may help reduce variability. Artificial intelligence may also support more consistent recognition, particularly among non-expert endoscopists, but such systems require broader validation across different populations and clinical settings (Chen et al., 2024; Shi et al., 2023).

Guideline-Related and System-Level Factors

AAG recognition is also affected by differences between international guidelines. Current guidelines agree on the importance of histological confirmation and risk-based surveillance, but they differ in how specifically they address AAG as a distinct endoscopic entity. The American Gastroenterological Association emphasizes topographic biopsies and histological confirmation but provides limited disease-specific visual criteria for AAG (Shah et al., 2021). The European MAPS III guideline focuses on gastric precancerous conditions, staging, surveillance, and virtual chromoendoscopy, but it approaches atrophic gastritis mainly through a cancer-prevention framework rather than an AAG-specific diagnostic framework (Dinis-Ribeiro et al., 2025). Japanese endoscopic literature provides more detailed descriptions of AAG-specific endoscopic features, including early-stage diagnostic challenges (Kamada et al., 2023; Kishino & Nonaka, 2022).

This lack of harmonization creates uncertainty in practice. A clinician following one guideline may prioritize histological staging and surveillance; another may focus on vitamin B12 deficiency as the trigger for investigation; another may use AAG-specific endoscopic criteria. As a result, the likelihood of diagnosis may depend on the clinical setting, local training, and the guideline tradition followed by the endoscopist. This is a system-level diagnostic gap.

AAG therefore requires clearer integration across guidelines. Endoscopy should not be viewed only as a confirmatory procedure after anemia or vitamin B12 deficiency is established. It should also be understood as a diagnostic opportunity in patients with suspicious corpus-predominant mucosal changes, unexplained iron deficiency, autoimmune comorbidity, persistent dyspeptic symptoms, hypergastrinemia, or suggestive serology. Standardized endoscopic criteria, biopsy protocols, and reporting templates could reduce diagnostic inconsistency and improve early recognition.

The endoscopic under-recognition of AAG results from a combination of subtle disease biology and modifiable clinical practice factors. Early mucosal changes may be difficult to see, and overlap with *H. pylori*-associated gastritis may obscure the diagnosis. However, many missed cases are also related to limited awareness, inadequate inspection, non-systematic biopsy strategies, inconsistent reporting, and guideline fragmentation. These factors indicate that AAG is not only an autoimmune gastric disease but also a quality-of-endoscopy challenge. Improving recognition requires better training, systematic biopsy practice, standardized reporting, and greater use of enhanced imaging and decision-support technologies.

Available and Emerging Technologies for Improving Endoscopic Recognition

The diagnostic gap in autoimmune atrophic gastritis (AAG) raises an important practical question: can available or emerging endoscopic technologies improve recognition before or alongside histological confirmation? Conventional white-light endoscopy remains the foundation of upper gastrointestinal examination, but its limitations are evident in early or subtle AAG. Because the disease often presents as diffuse background mucosal change rather than as a discrete lesion, enhanced visualization and decision-support tools may have particular value. However, these technologies should be understood as adjuncts to, rather than replacements for, careful inspection, clinical suspicion, and systematic biopsy protocols.

Image-Enhanced Endoscopy

Image-enhanced endoscopy has become increasingly important in the evaluation of gastric precancerous conditions. Narrow-band imaging (NBI), blue laser imaging, linked color imaging, and other virtual chromoendoscopy techniques improve visualization of mucosal and vascular patterns by enhancing contrast between epithelial structures and superficial vessels. These techniques may help identify gastric atrophy, intestinal metaplasia, and subtle mucosal abnormalities that are less apparent under standard white-light endoscopy (Dinis-Ribeiro et al., 2025; Rokkas & Ekmektzoglou, 2023).

The strongest evidence for NBI relates to the detection of gastric intestinal metaplasia and other premalignant gastric changes rather than AAG specifically. A systematic review and meta-analysis reported that NBI has high specificity for gastric intestinal metaplasia, suggesting that it may be useful for targeted assessment of premalignant mucosal patterns (Rokkas & Ekmektzoglou, 2023). Earlier evidence also showed that NBI, particularly when combined with magnification, improves visualization of mucosal pit patterns and microvascular architecture compared with white-light endoscopy alone (Zhang et al., 2014). These findings are relevant to AAG because advanced autoimmune gastritis often produces atrophy and intestinal metaplasia in the corpus.

Nevertheless, evidence directly evaluating NBI for AAG-specific recognition remains limited. AAG has a characteristic topographic distribution, especially corpus-predominant atrophy with relative antral sparing, but this pattern is not always easily captured by focal enhanced imaging. Image-enhanced endoscopy may improve detection of atrophy or intestinal metaplasia, but it does not independently establish autoimmune etiology. Therefore, its value in AAG lies mainly in improving mucosal characterization, guiding targeted biopsies, and supporting more accurate staging when combined with systematic biopsy and clinical-serological assessment.

Magnifying Endoscopy

Magnifying endoscopy allows closer examination of gastric pit patterns and microvascular structures. In AAG, magnification may reveal closely arranged round or oval pits in the atrophic corpus, as described in endoscopic studies of autoimmune gastritis (Yagi et al., 2012). Such findings may help distinguish autoimmune corpus atrophy from other forms of chronic gastritis, especially when interpreted together with the distribution of atrophy.

However, magnifying endoscopy has practical limitations. Its diagnostic value depends heavily on operator expertise, adequate mucosal preparation, stable imaging, and familiarity with specific gastric mucosal patterns. In less experienced hands, interpretation may vary substantially. This is particularly important because interobserver variability is already a recognized problem in the endoscopic grading of gastric atrophy (Kawamura et al., 2015). Magnification may therefore improve diagnostic precision in expert centers, but its broader impact depends on training, standardization, and reproducible criteria.

For AAG, magnifying endoscopy should be viewed as a potentially useful tool for selected cases rather than as a universal diagnostic solution. It may be most helpful when conventional endoscopy suggests corpus-predominant atrophy, when the distinction from *Helicobacter pylori*-associated

gastritis is uncertain, or when enhanced mucosal characterization is needed before biopsy. However, histology remains essential.

Virtual Chromoendoscopy and Guideline-Based Practice

Recent guideline developments support a stronger role for virtual chromoendoscopy in the assessment of gastric precancerous conditions. The MAPS III guideline recommends high-quality endoscopy with virtual chromoendoscopy for improved diagnosis and staging of atrophy and intestinal metaplasia (Dinis-Ribeiro et al., 2025). This recommendation is important because it shifts endoscopic practice from simple lesion detection toward systematic evaluation of the background gastric mucosa.

In the context of AAG, this shift is highly relevant. The diagnostic problem is not only the failure to detect tumors or focal lesions, but also the failure to recognize the premalignant mucosal field in which such lesions may develop. Virtual chromoendoscopy may improve recognition of atrophic borders, corpus mucosal thinning, intestinal metaplasia, and subtle vascular changes. It may also help endoscopists decide where targeted biopsies should be added to systematic mapping biopsies.

However, enhanced imaging cannot compensate for poor procedural technique. If the stomach is inadequately cleaned, insufficiently insufflated, or inspected too quickly, image-enhanced modalities will have limited value. Similarly, if biopsies are not taken according to a topographic protocol, enhanced visualization alone will not provide the histological confirmation required for diagnosis. Therefore, virtual chromoendoscopy should be embedded within a broader quality framework that includes adequate inspection time, complete gastric visualization, photographic documentation, and adherence to the updated Sydney System.

Artificial Intelligence-Assisted Endoscopy

Artificial intelligence (AI) represents one of the most promising emerging strategies for reducing missed diagnoses in gastrointestinal endoscopy. AI systems have already been developed for detecting gastric cancer, *H. pylori* infection, chronic atrophic gastritis, and other gastric mucosal abnormalities. In chronic atrophic gastritis more broadly, a meta-analysis reported high pooled sensitivity and specificity for AI-assisted endoscopic diagnosis, suggesting that machine-learning systems may help standardize recognition and reduce observer-dependent variability (Shi et al., 2023).

More recently, AI systems have begun to focus specifically on autoimmune gastritis. Chen et al. (2024) reported a multicenter study of an endoscopic AI system designed to assist in the diagnosis of autoimmune gastritis. The study suggested that AI may perform comparably to expert endoscopists and may improve diagnostic sensitivity among non-expert endoscopists when used as an assistive tool. This is especially relevant because AAG recognition depends on identifying subtle topographic and mucosal patterns that may be inconsistently recognized in routine practice.

The potential advantages of AI in AAG are several. First, AI may reduce interobserver variability by applying consistent visual criteria across examinations. Second, it may support non-specialist endoscopists in community settings, where exposure to AAG may be limited. Third, AI may function as a real-time prompt, encouraging the endoscopist to inspect the corpus more carefully, obtain appropriate biopsies, or consider autoimmune gastritis in the differential diagnosis. Fourth, future AI systems may combine endoscopic images with clinical data, serological markers, histology, and electronic health records to improve risk stratification.

Despite this promise, AI should not be presented as a definitive solution at this stage. Several limitations remain. Many AI systems are trained on datasets from specific populations or expert centers, which may limit generalizability to other regions and lower-prevalence settings. Performance may decline when image quality is poor, when disease is early or atypical, or when mixed etiologies such as AAG and previous *H. pylori* infection coexist. AI systems also require external validation, prospective

testing, integration into clinical workflow, and evaluation of their effect on actual patient outcomes rather than diagnostic accuracy alone.

Another important limitation is the low-prevalence effect. Even highly sensitive AI systems may generate false-positive alerts when applied broadly in populations where AAG is uncommon or under-suspected. For this reason, AI may be most effective when combined with risk-based case selection, including unexplained iron deficiency, vitamin B12 deficiency, autoimmune thyroid disease, hypergastrinemia, positive anti-parietal cell antibodies, or suspicious corpus-predominant endoscopic findings. In this model, AI would not replace the clinician but would strengthen decision-making in patients with a meaningful pre-test probability of AAG.

Integrated Diagnostic Strategy

The most realistic approach to improving AAG recognition is not reliance on a single technology, but integration of multiple diagnostic strategies. High-quality white-light endoscopy should remain the baseline. Image-enhanced endoscopy can improve visualization of atrophy and intestinal metaplasia. Magnification can support detailed mucosal assessment in selected cases. AI may provide real-time decision support and reduce variability. However, all of these tools must be combined with systematic biopsy protocols and clinical-serological interpretation.

A practical diagnostic pathway would include careful assessment of the distribution of gastric atrophy, attention to corpus-predominant changes, use of virtual chromoendoscopy when available, systematic biopsies according to the updated Sydney System, separate labeling of biopsy specimens, testing for *H. pylori*, and evaluation of autoimmune markers when AAG is suspected. In patients with unexplained iron deficiency, vitamin B12 deficiency, autoimmune thyroid disease, or hypergastrinemia, the threshold for mapping biopsies should be lower, even if endoscopic findings are subtle.

Thus, technology can help bridge the diagnostic gap, but only within a quality-of-endoscopy framework. The central problem in AAG is not merely that the disease is difficult to see. It is that subtle mucosal changes are often not interpreted, biopsied, reported, or followed up in a standardized manner. Available and emerging technologies can improve recognition, but their effectiveness depends on training, guideline integration, biopsy discipline, and validation in real-world clinical settings.

Discussion

This review highlights a central and clinically relevant problem: autoimmune atrophic gastritis (AAG) is often diagnosed late because endoscopic recognition does not consistently precede or guide histological confirmation. Although AAG has characteristic pathological and clinical features, its endoscopic diagnosis remains unreliable in routine practice. The evidence reviewed suggests that this gap is not explained by disease rarity alone. Rather, AAG should be understood as a quality-of-endoscopy problem shaped by subtle disease presentation, limited endoscopist awareness, inconsistent biopsy strategies, interobserver variability, and incomplete guideline integration.

The first major finding is that the biology of AAG itself contributes to under-recognition. Early disease may produce minimal or nonspecific mucosal changes, while histological atrophy may already be present. This creates a diagnostic challenge because endoscopists may not suspect AAG when the mucosa appears normal or only mildly abnormal. In advanced disease, the endoscopic pattern becomes more recognizable, particularly when corpus-predominant atrophy, loss of rugal folds, mucosal pallor, and visible vessels are present (Kamada et al., 2023; Kishino & Nonaka, 2022). However, waiting until these features become obvious defeats the purpose of early diagnosis. Since clinical complications such as iron deficiency, vitamin B12 deficiency, neurological impairment, and neuroendocrine tumors may develop over time, delayed recognition has direct consequences for patient care (Castellana et al., 2024; Lenti et al., 2020).

A second important finding is that AAG is frequently obscured by its overlap with *Helicobacter pylori*-associated gastritis. In theory, AAG and *H. pylori*-associated atrophic gastritis have different topographic patterns: AAG is typically corpus-predominant, whereas *H. pylori*-associated atrophy often begins in the antrum. In practice, however, this distinction may be difficult to apply. Advanced *H. pylori* gastritis, post-eradication changes, mixed etiologies, or regression of antral atrophy may create a pattern that resembles autoimmune corpus atrophy (Dottori et al., 2024; Nishizawa et al., 2021). This overlap can lead to two types of diagnostic error: AAG may be mistaken for *H. pylori*-related gastritis, or *H. pylori*-associated atrophy may be misclassified as autoimmune disease. Both errors matter because they affect treatment, surveillance, and evaluation for associated autoimmune and neoplastic risks.

The findings also suggest that missed AAG is partly a modifiable human-factor problem. Many endoscopists may still associate AAG mainly with pernicious anemia or advanced disease, rather than considering it in patients with unexplained iron deficiency, dyspepsia, autoimmune thyroid disease, hypergastrinemia, or subtle corpus-predominant mucosal change. This limited awareness reduces the likelihood of targeted suspicion and systematic biopsy. Evidence from studies of gastric atrophy classification indicates that endoscopic agreement is only moderate even among experienced endoscopists, but improves with structured training (Eshmuratov et al., 2019; Kawamura et al., 2015). Therefore, improving endoscopist education may be one of the most practical interventions for reducing missed AAG. Image-based teaching modules, standardized examples of early and advanced AAG, and consensus reporting terminology could help transform AAG recognition from an expert-dependent skill into a reproducible component of routine endoscopy.

Procedure-related factors are equally important. AAG is not usually diagnosed by identifying a single focal lesion; it is recognized by evaluating the background gastric mucosa and its topographic distribution. This requires adequate mucosal cleansing, insufflation, careful inspection of the corpus and fundus, comparison with the antrum, and appropriate photographic documentation. If endoscopy is performed primarily as a lesion-detection procedure, diffuse atrophic patterns may be overlooked. This is especially problematic in settings where biopsy is performed only when focal abnormalities are seen.

The updated Sydney System remains one of the most important safeguards against missed diagnosis. Because AAG depends on topographic interpretation, biopsies must be taken from appropriate gastric sites and submitted in separately labeled containers. If corpus biopsies are omitted, if specimens are combined in one container, or if the pathology report does not preserve anatomical site information, the autoimmune pattern may be missed (Shah et al., 2021). Thus, the diagnostic gap is not only visual but also procedural. Even excellent histopathology cannot compensate for inadequate sampling. Conversely, systematic biopsies can reveal AAG even when endoscopic findings are subtle or nonspecific.

Guideline differences represent a system-level contributor to diagnostic inconsistency. Current guidelines generally agree that histological confirmation and staging are essential, but they differ in the emphasis placed on AAG-specific endoscopic recognition. The American Gastroenterological Association emphasizes biopsy and histological confirmation, while the European MAPS III guideline focuses on staging, surveillance, and virtual chromoendoscopy for gastric precancerous conditions (Dinis-Ribeiro et al., 2025; Shah et al., 2021). Japanese endoscopic guidance provides more detailed descriptions of AAG-specific visual features, including early-stage diagnostic challenges (Kamada et al., 2023). These frameworks are individually useful, but none fully resolves the practical problem of when and how the endoscopist should suspect AAG before histology. More harmonized guidance is needed, particularly regarding endoscopic suspicion criteria, biopsy indications, and reporting standards.

The role of technology should be interpreted with cautious optimism. Image-enhanced endoscopy, including narrow-band imaging and virtual chromoendoscopy, can improve visualization of atrophy and intestinal metaplasia and is increasingly recommended for the assessment of gastric precancerous conditions (Dinis-Ribeiro et al., 2025; Rokkas & Ekmektzoglou, 2023). However, its AAG-specific evidence base remains limited. These modalities can improve mucosal characterization and guide

biopsies, but they do not independently establish autoimmune etiology. Their value depends on integration with clinical context, serology, *H. pylori* testing, and histology.

Artificial intelligence may become a particularly useful adjunct because it directly addresses interobserver variability and limited expertise. Recent studies suggest that AI-assisted endoscopy can achieve high diagnostic performance for chronic atrophic gastritis and may support the recognition of autoimmune gastritis, especially among non-expert endoscopists (Chen et al., 2024; Shi et al., 2023). In principle, AI could function as a real-time prompt to inspect the corpus more carefully, consider AAG in the differential diagnosis, and obtain appropriate mapping biopsies. However, AI should not be presented as a replacement for clinical reasoning or biopsy protocols. Its performance must be validated in diverse populations, including Western and low-prevalence settings, and its real-world value should be assessed by whether it reduces diagnostic delay, improves biopsy practice, and changes patient outcomes.

The clinical implications of improved recognition are substantial. Earlier identification of AAG allows evaluation and treatment of iron and vitamin B12 deficiency, assessment for autoimmune comorbidities, measurement of gastrin and pepsinogen markers when appropriate, and surveillance for type I gastric neuroendocrine tumors and advanced premalignant lesions. Because some complications of delayed diagnosis may be irreversible, particularly neurological complications of vitamin B12 deficiency, earlier recognition has value beyond cancer prevention (Lenti et al., 2020). Moreover, recognizing AAG may prevent inappropriate or repeated treatment for presumed *H. pylori* gastritis and may guide more individualized follow-up.

This review has several limitations. First, it was designed as a structured narrative review rather than a systematic review or meta-analysis. Therefore, it did not include formal risk-of-bias assessment, quantitative pooling, or protocol registration. Second, the evidence base is uneven. There are relatively few studies directly measuring endoscopist awareness, diagnostic accuracy, or recognition of AAG in routine Western practice. Much of the argument regarding awareness and training is therefore inferred from related evidence on gastric atrophy and gastritis recognition. Third, many studies of endoscopic features and emerging technologies come from specialized centers or specific geographic regions, which may limit generalizability. Fourth, the role of AI remains promising but still insufficiently validated for broad clinical implementation.

Despite these limitations, the synthesis supports a clear practical conclusion. AAG diagnosis can be improved by reframing the disease as a recognizable and surveillable premalignant condition rather than as a rare cause of pernicious anemia. This requires a quality-oriented approach to endoscopy: systematic inspection of the gastric corpus and fundus, attention to topographic atrophy, routine use of mapping biopsies in suspected cases, separate labeling of specimens, structured reporting, and greater use of enhanced imaging when available. Training and guideline harmonization are likely to have immediate impact, while AI-assisted systems may become valuable tools once externally validated and integrated into real-world workflows.

In summary, the diagnostic delay of AAG reflects a gap between what endoscopy can theoretically detect and what routine practice consistently recognizes. Closing this gap requires not only better technology but also better endoscopic discipline, clearer diagnostic criteria, and stronger integration between clinical suspicion, endoscopic findings, biopsy strategy, and histopathology.

Conclusion and Recommendations

Autoimmune atrophic gastritis (AAG) remains under-recognized despite the routine availability of upper gastrointestinal endoscopy. This review shows that the diagnostic gap is not explained solely by the insidious nature of the disease. Rather, delayed recognition reflects a combination of subtle early mucosal findings, overlap with *Helicobacter pylori*-associated gastritis, limited endoscopist awareness, inadequate biopsy strategies, interobserver variability, and incomplete guideline harmonization. For this reason, AAG should be understood not only as an autoimmune gastric disorder but also as a quality-of-endoscopy challenge.

The clinical importance of this diagnostic gap is substantial. Missed or delayed recognition may postpone the diagnosis of iron deficiency, vitamin B12 deficiency, pernicious anemia, neurological complications, autoimmune comorbidities, and type I gastric neuroendocrine tumors. Since some complications may become irreversible and AAG is associated with premalignant gastric changes, earlier endoscopic suspicion and histological confirmation are essential for appropriate surveillance and long-term risk reduction.

Several practical recommendations follow from this review. First, endoscopic training programs should include dedicated modules on AAG, with emphasis on corpus-predominant atrophy, reverse atrophy patterns, early subtle mucosal changes, and differentiation from *H. pylori*-associated gastritis. Second, endoscopists should apply systematic biopsy protocols in suspected cases, particularly the updated Sydney System, with separate labeling of antral, incisural, and corpus specimens. Third, endoscopic reports should describe the topography and severity of atrophy rather than using nonspecific terms such as "gastritis" alone. Fourth, image-enhanced endoscopy should be incorporated when available to improve visualization of atrophic and metaplastic mucosal patterns. Fifth, international guidelines should provide clearer AAG-specific criteria for endoscopic suspicion, biopsy indications, reporting, and surveillance.

Artificial intelligence may become an important supportive tool for reducing missed diagnoses and interobserver variability, especially among non-expert endoscopists. However, AI-assisted systems require further external validation in diverse populations and should be integrated into clinical practice only as adjuncts to careful inspection, clinical judgment, and histological confirmation. Future research should focus on measuring real-world endoscopist recognition accuracy, validating early-stage endoscopic criteria, assessing the effectiveness of training interventions, and evaluating whether AI-assisted endoscopy can reduce diagnostic delay and improve patient outcomes.

Overall, improving AAG diagnosis requires a shift from passive recognition of advanced disease to active, quality-driven detection of premalignant gastric mucosal change. Earlier suspicion, standardized biopsy practice, structured reporting, and appropriate use of enhanced imaging and decision-support technologies can help close the gap between endoscopic examination and histological diagnosis.

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