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Chronic Atrophic Gastritis and Intestinal Metaplasia: A Latin American Perspective

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Gastric cancer (GC), a significant cause of mortality globally, is the leading cause of cancer-related deaths among Latin American men. GC is usually diagnosed at an advanced stage; therefore, therapeutic options are limited, and prognosis is poor. *Helicobacter pylori* infection remains the primary risk factor for GC; therefore, primary prevention directed toward diagnosis and treatment ("test-and-treat" strategy) is important. Western medicine guidelines recommend esophagogastroduodenoscopy (EGD) for at-risk individuals aged >40 years with regular surveillance in patients with gastric premalignant conditions (GPMC). However, limited availability of EGD in Latin America necessitates development of risk stratification tools to minimize the endoscopic burden. Results from the Chilean "Endoscopic Cohort and Histological Operative Link on Gastric Assessment (OLGA) Staging" (ECHOS study), propose endoscopic surveillance of advanced GPMC (OLGA/Operative Link for Gastric Intestinal Metaplasia [OLGIM] stages III–IV) with reliable risk stratification to facilitate early GC detection. Ensuring high-quality EGD and enhanced diagnostic yield of GPMC is essential. GPMC grading tools, such as the Kimura-Takemoto or Endoscopic Grading of Gastric Intestinal Metaplasia classification, should be incorporated into the regular risk assessment protocol. However, obtaining mapping gastric biopsies using standardized methods such as the updated Sydney System biopsy protocol, followed by grading of chronic atrophic gastritis with or without intestinal metaplasia using the OLGA and OLGIM staging systems are preferred for GC risk stratification. Recent GC prevention strategies recommended in Chile include a "test-and-treat" approach for *H. pylori* in individuals aged 35–44 years and combined *H. pylori*/pepsinogen I–II serology and EGD evaluation in patients aged >45 years to optimize the limited preventive resources available in the region.

Keywords Gastrointestinal endoscopy; Stomach neoplasm; *Helicobacter pylori*.

INTRODUCTION

Gastric cancer (GC), a major cause of cancer mortality worldwide, accounts for an estimated 95000 deaths in Latin America.[1] With an incidence rate of 25.7 per 100000 inhabitants, the Chilean population showed an intermediate risk of GC between 2009 and 2018,[1] and GC was the leading and third leading contributor to cancer-related deaths among men and women, respectively.[2] Although variations in incidence rates are documented across regions globally, intra-regional hetero-

geneity has been identified.[1] Therefore, various strategies tailored to local prevalence are implemented globally to control GC or to facilitate detection in the incipient stages. These strategies usually target well-known risk factors such as *Helicobacter pylori* infection, considering its established role in GC development.[3,4] GC is usually diagnosed in advanced stages,[5] which not only limits therapeutic alternatives but also shortens survival.[6]

The current guideline for GC prevention in Chile recommends esophagogastroduodenoscopy (EGD) for evaluation of GC in individuals aged >40 years with upper gastrointestinal symptoms, such as epigastralgia that persists over 14 days.[7] In accordance with this recommendation, the National Association of Endoscopy of Chile advises risk stratification of GC using the Operative Link on Gastritis Assessment (OLGA) or Operative Link on Gastric Intestinal Metaplasia (OLGIM) staging systems in patients aged >40 years and endoscopic surveillance in patients with high-risk gastric premalignant conditions (GPMC) such as OLGA/OLGIM stages III–IV,[8] which is similar to the management of precancerous conditions and lesions in the stomach (MAPS) II European guideline.[9] However, owing to limited availability of EGD in Chile,[10] development of risk stratification tools to optimize resource utilization is important. High-quality evaluation can improve the diagnostic yield of GPMC, which involves virtual chromoendoscopy,[11] such as blue laser imaging (BLI)[12] or narrow-band imaging (NBI),[13] as well as application of classifications including the Kimura-Takemoto (KT)[14,15] classification for chronic atrophic gastritis (CAG) and the Endoscopic Grading of Gastric Intestinal Metaplasia (EGGIM)[16,17] scoring system within EGD protocols. Additionally, biopsies should be obtained using standardized methods such as the updated Sydney system biopsy protocol,[18] followed by comprehensive evaluation using the OLGA[19] or OLGIM staging systems,[20] respectively.

In a recent study, we presented the following updated GC prevention strategy for Chile:[21] We propose a "test-and-treat" approach for *H. pylori* in individuals aged 35–44 years and combined *H. pylori*/pepsinogen (PG) I–II serology and EGD for patients aged >45 years, with further endoscopic surveillance in patients with high-risk GPMC. We expect this strategy will ensure optimization of the scarce preventive resources available in the region. However, this approach may be debatable, and new evidence may provide better and more accurate tools to design an effective preventive strategy.

In view of the lack of a definitive evidence-based approach, we review the Latin American perspective of GC prevention and assessment and discuss various alternatives adopted worldwide.

RISK FACTORS OF GASTRIC CANCER

Despite high incidence rates, a declining trend in GC is reported worldwide.[22,23] However, the future course remains uncertain considering rapid population aging and an increase in GC incidence among younger populations in both low- and high-risk countries.[24,25] Despite potential links with autoimmune gastritis[24,26] and an increase in diffuse-type GC reported in the young western population, the true risk remains unclear.[27] In contrast, the role of *H. pylori* in GC is extensively documented in the literature,[28-30] and this organism is acknowledged as a carcinogen over decades.[4] The decline in the estimated worldwide prevalence of *H. pylori* from 1980 to 2022[31] has potentially contributed to the decrease in GC rates, which is attributable to improved hygiene and sanitation, although these factors are implicated as potential contributors to the varying *H. pylori* prevalence across regions, with the highest prevalence observed in African countries.[32] Latin America is identified as a geographical area with high prevalence rates ranging between 64.0% and 75.0%.[32] Specifically, the historical seroprevalence of *H. pylori* infection in Chile is >70.0%;[33] however, in our recent study, we observed a significant decline in this rate, with prevalence as low as 29.0%.[34] In Latin America, high prevalence rates are particularly recorded among countries along the western Andes Mountains ("the Andes Enigma"). A high GC risk is identified in Andean regions of Latin America located at higher altitudes in contrast to that in regions at sea level (the "Altitude enigma"). It is hypothesized that these differences may be explained by dissimilarities in diet, salt intake, *H. pylori* prevalence, prevalence of *H. pylori* CagA-positive strains, and other gastrointestinal co-infections.[35]

GASTRIC PREMALIGNANT CONDITIONS

Gastric adenocarcinoma (GA), the most common type of GC, is preceded by a preneoplastic histopathological cascade originally described by Correa et al.[36] in 1975 in a Colombian cohort. *H. pylori* infection serves as the primary initiator of carcinogenesis,[37] although other triggers including autoimmunity are known contributors. Drivers of inflammation in chronic superficial gastritis may lead to CAG with or without intestinal metaplasia (IM) in some patients; these conditions are commonly categorized as gastric preneoplastic conditions (GPNC). Interactions between host, microbial, and environmental factors (which are incompletely understood) trigger neoplastic transformation to low- or high-grade dysplasia (LGD and HGD, respectively) and subsequently GA in a few patients with GPNC.[38-40] This stepwise cascade may occur over

several years before onset of early GA, which enables surveillance and early diagnosis of GA. However, most patients with CAG and IM do not show progression to dysplasia or GA.

IM may present as a complete or incomplete histological type,[30,41] which is associated with a higher risk of GC[39,42] and is considered a mild form of dysplasia.[43] Extensive IM, defined as involvement of both the antrum and corpus in contrast to lesions restricted to the antrum, is also associated with an increased risk of GC.[39] Gastric dysplasia is characterized by a neoplastic phenotype with regard to cell morphology and architectural organization[28] and is often classified into LGD or HGD.[44] HGD is correlated with poor prognosis with regard to GC progression,[40] and therefore, various guidelines recommend resection of HGD and focal LGD followed by close surveillance to detect early-stage post-resection GC.[8,9] In contrast, emerging diagnostic and stratification tools for both CAG and IM have facilitated adoption of a surveillance strategy to mitigate the risk of malignancy and alleviate the cost-effective burden through comprehensive evaluation. Nevertheless, scarce resources to perform biopsies, shortage of pathologists, poor sample standardization, and discrepancies among pathologists are among the limitations in Latin America. The future trajectory involves improved training for pathologists and integration of artificial intelligence (AI) tools to aid with diagnosis and decision-making.

DIAGNOSIS OF CHRONIC ATROPHIC GASTRITIS AND INTESTINAL METAPLASIA

Serological and non-invasive biomarkers

Serum PG testing has emerged as a useful non-invasive method for evaluation of GA, IM, and GC.[45-47] PGs serve as proenzymes for pepsin and are categorized biochemically and immunologically into PGI and PGII. Both are secreted by the chief and mucous neck cells in the fundic glands;[48] however, PGII is additionally secreted by cells in the pyloric and Brunner's glands.[49] Atrophic changes result in loss of normal cells and a decrease in PGI levels; however, PGII levels remain stable, with a consequent reduction in the PGI:PGII ratio (PGR).[45] Although a specific threshold for PGI and PGR is not established, 70 μg/L and a ratio of 3, respectively show acceptable sensitivity and specificity for GC.[46] A meta-analysis that investigated the diagnostic accuracy of serum PGs for detection of GA and GC reported sensitivity and specificity of 0.69 (95% confidence interval [CI] 0.55–0.80) and 0.88 (95% CI 0.77–0.94), respectively for GA and 0.69 (95% CI 0.60–0.76) and 0.73 (95% CI 0.62–0.82), respectively for GC. Furthermore, the combination of PGI and PGR yielded the highest area under the receiver operating characteristic curve (AUC) for both CAG and GC. However, heterogeneity among cutoff values, quantification methods for PGs, and geographical areas across studies emphasizes the need for prospective studies to validate these results.[46] Furthermore, only few reports published in the Latin American literature validate the role of PGI and PGII; therefore, the generalizability of these findings is limited in our country.

In addition to PGs, other serum markers including trefoil factor 3 (TFF3), gastrin-17, and anti-*H. pylori* antibodies are available to evaluate gastric mucosal changes.[50-54] In a recent study, we observed a correlation between serum TFF3 levels and invasive GC; however, no correlation was observed with regard to GPNC such as IM.[54] Gastrin-17 is a suggested biomarker for CAG and GC because an increased gastrin level was associated with GC,[50,51] and anti-*H. pylori* antibodies were associated with premalignant conditions.[52] Recent studies have reported the usefulness of PGI, PGII, PGR, gastrin-17, and immunoglobulin (Ig)G anti-*H. pylori* combinations (GastroPanel) to identify high-risk individuals to undergo subsequent EGD,[52,53] in addition to proposed prediction rules for application to high-risk populations based on these serological markers[51] to maximize the yield and usefulness of EGD, with attention to the cost-benefit ratio.

Other non-invasive serological markers, including decreased serum ghrelin[46] and microRNA levels are proposed for GPNC evaluation.[55] However, these are not currently used considering limited evidence to confirm their results. Resources dedicated to GC prevention are currently limited in Latin America.[56] Application of biomarkers may facilitate non-invasive early-stage diagnosis, risk stratification for patients who require EGD, and optimization of surveillance frequency for GPNC. Owing to scarce laboratory resources, serological or enzyme-linked immunosorbent assay tests are preferred over more intricate molecular tools.

Esophagogastroduodenoscopy

EGD screening has reduced the GC incidence; therefore, this procedure is preferred for gastric evaluation.[57] However, heterogeneity in gastric evaluation and consequent missed diagnoses are concerns associated with EGD[58-60] owing to inability to perform a systematic gastric examination. A meta-analysis in 2016 highlighted that approximately 1 in 10 cases of GC were potentially overlooked, particularly those with lesions involving the greater curvature of the body and the antrum and blind spots including the incisura/lesser curvature and cardia.[59] To address this drawback, comprehensive training is important to enhance proficiency in performing EGD procedures and to improve GPNC detection rates.[60] Thorough

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cleaning, insufflation, and visualization of the gastric mucosa can improve this rate[61-63] and facilitate accurate evaluation via utilization of standardized score systems such as the Toronto Upper Gastrointestinal Cleaning Score.[64] Mucolytic agents such as pronase are extensively used for EGD preparation in Asian countries[65] to improve mucosal visibility;[66] however, this strategy is unavailable in Western countries,[67] and simethicone+N-acetylcysteine is used as an anti-foaming agent for EGD preparation. A randomized controlled trial performed at our hospital reported that simethicone+N-acetylcysteine administration improved visibility during EGD.[68] The results show that the available alternative in Latin America has good efficacy and is beneficial despite absence of optimal resources, which highlights the need to more actively promote its use. Western countries recommend 6-hour fasting for solids; however,[63] a pre-EGD midnight fast is common in Latin America, in contrast to the 2-hour clear liquid fast regimen used in Asian nations. Recent studies report that reduced fasting duration does not affect patient comfort, safety, or endoscopic visibility during EGD,[69] which suggests the need to revise our current pre-EGD patient preparation practices. Additionally, extended inspection of the gastric mucosa to >7 min is associated with an improved detection rate of high-risk lesions.[61] Therefore, an optimal inspection time of 7–8 min is recommended to maximize lesion detection rates.[11,62,63]

Image-enhanced endoscopy (IEE) has emerged as a novel method to improve detection rates compared with conventional white-light endoscopy (WLE), which shows limited correlation with histopathological findings of GPNC.[70,71] Virtual chromoendoscopy improves the diagnostic accuracy of early-stage GC and GPMC,[72] including BLI, linked color imaging (LCI) (Fujifilm, Japan) and NBI (Olympus Medical Systems, Japan).[60,73] BLI involves use of blue laser to penetrate the mucosa and excite hemoglobin to enhance mucosal surface visibility,[74] and LCI expands red coloration and accentuates hemoglobin contrast[75] to produce brighter images that improve lesion visibility.[76,77] NBI uses a narrow bandwidth light filter to increase the contrast between mucosal microstructures and microvessels[75] and shows high concordance with gastric histology in combination with WLE[13] and yields diagnostic results comparable to those of BLI.[77] These results highlight the need to train endoscopists in these techniques to enhance proficiency in EGD. Furthermore, AI has emerged as a promising area of research; AI can identify GPNC with accuracy levels comparable to those of expert assessments, using WLE or image-enhanced approaches.[78-81] Future studies should investigate the potential applications of AI in clinical practice.

The following EGD classifications have emerged as valuable tools for GPNC evaluation: 1) The KT classification[14] is

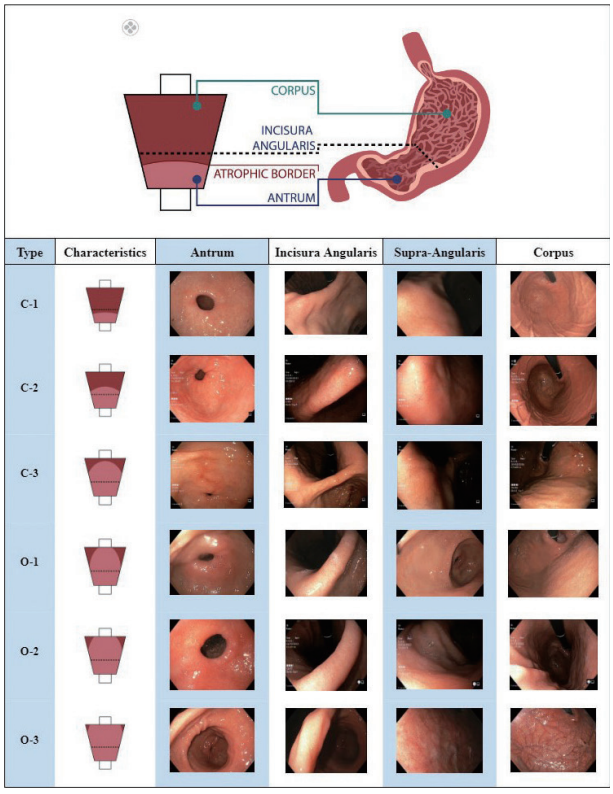


Fig. 1. The Kimura-Takemoto Classification with two subclasses as follows: "C" for closed-type and "O" for open-type. C-1: Atrophic changes are visible only in the antrum, without signs of corporal atrophy. C-2: An atrophic border is observed above the incisura angularis but below the midpoint of the lesser curvature of the stomach. C-3: An atrophic border is observed above the midpoint of the lesser curvature of the stomach; however, the anterior wall of the stomach is unaffected. O-1: An atrophic border is observed between the lesser curvature and anterior wall of the stomach. O-2: An atrophic border is observed in the anterior wall of the stomach. O-3: An atrophic border is observed between the anterior wall and greater curvature of the stomach. Adapted from Miwata et al. BMC Gastroenterol 2015;15:95.[111], under the terms of the Creative Commons License (CC BY).

used to stratify GA based on the observed site of the endoscopic border, and findings are categorized into six groups. Although the KT classification accurately predicts the GC risk in patients with advanced CAG (open type), further prospective studies are required in the Western population and particularly in the Latin American context to validate these results. Fig. 1 shows endoscopic images of the KT classification. 2) The EGGIM scoring system is used to evaluate IM using NBI,[16] and this score has been externally validated to predict the risk of OLGIM stages III/IV without performing biopsies.[17] This scoring system is based on thorough evaluation of the gastric mucosa and assigns a score ranging from 0 to 2 based on the extent of metaplasia across five different sites within the stomach, including the greater and lesser curvatures of the antrum, the incisura angularis, and the greater and lesser curvatures of the corpus.[16] Fig. 2 shows the EGGIM scoring system and

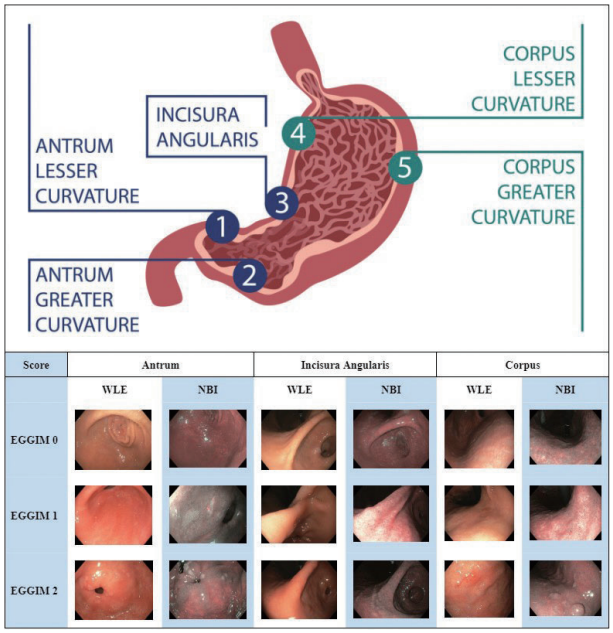


Fig. 2. The EGGIM score ranging from 0 to 10 is obtained following evaluation of GIM across the following five specific sites within the stomach: the greater and lesser curvature of the antrum, the incisura angularis, and the greater and lesser curvature of the corpus. GIM is categorized into the following grades: 0 for no GIM (EGGIM 0), 1 for GIM ≤30.0% (EGGIM 1), and 2 for GIM >30.0% (EGGIM 2). EGGIM, Endoscopic Grading of Gastric Intestinal Metaplasia; GIM, gastric intestinal metaplasia; NBI, narrow-band imaging; WLE, white-light endoscopy.

clinical images obtained using NBI. 3) The AB Yagi classification[82] initially categorized endoscopic features of the corporal gastric mucosa based on changes observed in mucosal patterns and vascularity on magnified imaging; these findings were correlated with histological features and active *H. pylori* infection, and four categories were defined ranging from normal mucosa to intense chronic gastritis. In 2007, the authors modified this classification to include two new categories to evaluate GA and IM.[83] These classifications show >90.0% diagnostic accuracy for *H. pylori* infection in B1, B2, and B3 categories.[84] Fig. 3 shows the endoscopic features and clinical images based on the Yagi classification.

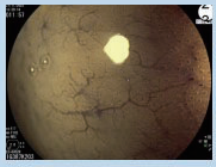
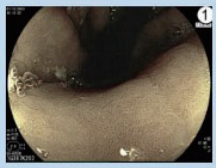
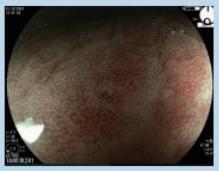
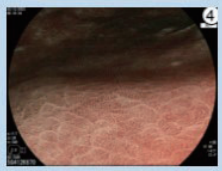
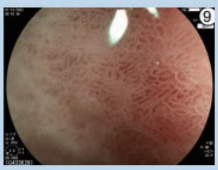
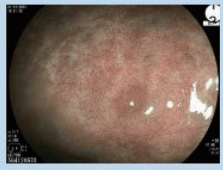
Grade	Characteristics	Endoscopic Magnified Visualization
B0	Uniform round pits with opened crypts surrounded by honeycomb-shaped subepithelial capillary network and collecting venules in star-like structures.	
B1	Uniform round pits with opened or closed crypts surrounded by a regular or mild irregular honeycomb-shaped subepithelial capillary network with no presence of collecting venules	
B2	Round or slightly dilated pits divided with opened or closed crypts, with dividing sulcis. Loss of honeycomb-shaped subepithelial capillary network with no presence of collecting venules.	
B3	Dilated pits with opened or closed crypts, with numerous dividing sulcis. Loss of honeycomb-shaped subepithelial capillary network with no presence of collecting venules.	
A1	Villous mucosal pattern, surrounded by coiled subepithelial capillary network with no presence of collecting venules.	
A2	Villous structures or loss of mucosal pattern, with irregularly narrowed coiled subepithelial capillary network with no presence of collecting venules.	

Fig. 3. The Yagi AB classification categorizes the endoscopic features of the corporal gastric mucosa based on changes observed in mucosal patterns and vascularity using magnification and correlation with histopathological features, as well as detection of active *H. pylori* infection to define six categories ranging from normal mucosa to chronic atrophic gastritis and intestinal metaplasia.

Gastric biopsy collection and histopathological risk assessment

Evidence suggests that IEE performed by experienced endoscopists may potentially obviate the need for biopsies; however,[16,17] IEE availability is limited and performance among endoscopists varies widely.[85] Therefore, histopathological evaluation is regarded as the gold standard for GPNC detection and GC risk stratification. Obtaining an adequate number of representative biopsies is extremely important for accurate diagnosis, and multiple biopsies should be avoided to minimize high medical costs.[60] The updated Sydney system biopsy protocol is a suitable alternative to enhance the diagnostic yield.[18] Per this protocol, biopsies are obtained from five gastric locations as follows (Fig. 4A): two from the antrum (from both the greater and lesser curvatures, 3 cm from the pylorus), one from the incisura, and two from the body (from the lesser curvature, 4 cm proximal to the incisura and the mid portion of the greater curvature). Biopsies obtained based on this protocol are evaluated by pathologists using the OLGA and OLGIM staging systems. Both classification systems determine the extent of the condition, and scores ranging from 0 to II are assigned for each location, with an overall score from 0 to

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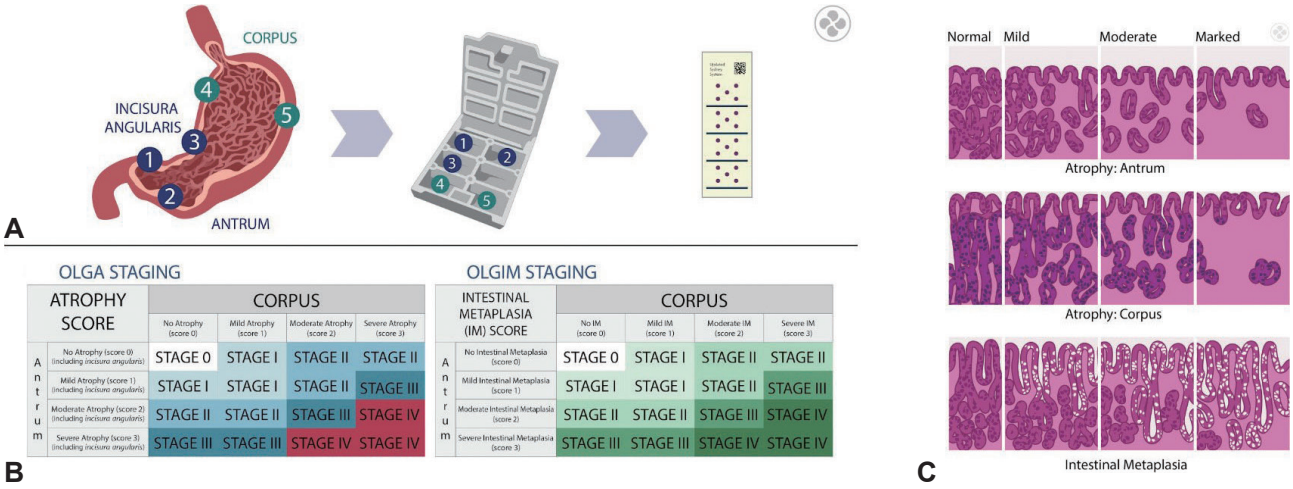

Fig. 4. Gastric mapping biopsies and histological evaluation. A: Sites of sample collection per the Sydney system biopsy protocol. B: The OLGA and OLGIM staging systems. C: Histopathological characteristics of chronic atrophic gastritis and intestinal metaplasia. OLGA, Operative Link for Gastritis Assessment; OLGIM, Operative Link for Gastric Intestinal Metaplasia Assessment.

IV. Higher scores with OLGA/OLGIM stages III/IV show a significant association with the GC risk,[86-88] which highlights the importance of risk assessment and subsequent follow-up protocols for secondary prevention. Fig. 4B and C show the OLGA and OLGIM classifications and histopathological characteristics of CAG and IM, respectively. Combined biopsies obtained via the Sydney protocol show nearly 100.0% sensitivity for *H. pylori* diagnosis[89] and are useful for detection and eradication.[90] Greater consensus and training for pathologists in addition to improved biopsy rates are needed in Latin America. We have implemented the use of cassettes for biopsy collection at our hospital (Fig. 4A) to reduce costs and improve organization of the samples for pathologists.[18]

RISK STRATIFICATION AND SURVEILLANCE

Various risks are associated with findings across endoscopic classifications. The KT classification is a reliable predictor of both current and future GC risk, showing a significant increase in detection rates of GC with progression of atrophy from closed- to open-type categories.[15] Recent retrospective studies have reported similar results.[91,92] Maric et al.[91] compared open- and closed-type KT, with a hazard ratio (HR) of 13.3 (95% CI 5.3–33.4) for dysplasia and 6.4 (95% CI 2.4–16.8) for progression to GC. Chen et al.[92] compared the same groups and reported that open-type KT showed high predictive ability for early-stage GC, with an adjusted odds ratio (OR) of 3.3 (95% CI 1.1–9.7). Long-term cohort studies have reported the usefulness of the classification as a valuable risk stratification tool.[93] This simple classification based on WLE may be applicable to the Latin American context, although validation in Western regions is necessary. Our findings suggest that we may observe fewer patients with the open-type category among the Chilean population and a higher percentage of patients with the C3 type (unpublished data), with more cases of GC involving the lesser curvature, which indicates the questionable role of this classification in the Latin American population and suggests the need for validation, particularly with regard to the classification of C3 as a risk category in Latin America.

The EGGIM classification score is another valuable tool for evaluation of patients with GPNC.[16,17] Externally validated by researchers in both a low-risk country (Italy) and a medium-to-high risk country (Portugal), the EGGIM score has shown consistency across diverse risk settings.[17] Using the OLGIM III/IV staging system as a gold standard, which indicates a high risk of GC,[86,88] an EGGIM score >4 showed sensitivity and specificity of 87.2% (95% CI 81.2%–91.7%) and 94.3% (95% CI 89.8%–97.1%), respectively, with slight improvement after excluding foveolar hyperplasia,[17] which potentially produces an endoscopic false-positive result for IM.[94] A recent meta-analysis supports this cutoff value, with a high OR of 7.46 (95% CI 2.06–23.05) for scores between 5–10 compared with scores 0–4, together with high concordance between OLGIM and scores 5–10, yielding an AUC of 0.97. However, specificity was heterogeneous among the included studies, which is primarily attributable to differences in the number of false-positive results and overestimation of patients with OLGIM stages 0–II. Therefore, it is suggested that the EGGIM score can successfully identify high-risk patients, and application of the EGGIM score may potentially serve as the initial step in risk stratification.[93] Despite the promising results observed with both the KT and EGGIM classifications, currently no follow-up strategies associated with these scores are available in the existing and pro-

posed guidelines.[9,21,95-98] Further studies are warranted to directly investigate the association between the EGGIM score and GC risk to develop appropriate surveillance strategies.

IM shows a high risk of malignant transformation, particularly in patients with incomplete or extensive IM.[39,41] Incomplete-type IM shows a higher risk of malignancy, with a relative risk (RR) of 1.7 (95% CI 0.8–3.7) and 3.33 (95% CI 1.96–5.64) for progression to gastric dysplasia and GC, respectively.[39] More recent meta-analyses support these findings, with the pooled RR for GC and dysplasia in patients with incomplete IM being 5.16 (95% CI 3.28–8.12) and 3.72 (95% CI 1.42–9.72), respectively.[99] Moreover, extension of IM is considered a risk factor for progression to malignancy,[39] with a higher risk of progression to GC in patients with extensive IM than in those with limited IM (RR 2.07 [95% CI 0.97–4.42]), although significance was not achieved owing to heterogeneous definitions of extensive IM or incomplete biopsy protocols described by the included studies.[41] Several guidelines recommend 3-year surveillance for patients with these characteristics, including diagnosis of IM and a family history of GC.[9,95-97]

The findings reported in the Colombian cohort,[100] which represents the longest prospective study in Latin American patients who were investigated after *H. pylori* eradication trials, are significant to understand the progression and reversibility of GPNC. The study with 20-year follow-up revealed that CAG may regress to a non-atrophic stage after at least 6 years of *H. pylori* eradication; however, IM is usually irreversible to less advanced stages, except in patients with limited or complete-type IM. The results highlight the significant role of *H. pylori* eradication in disrupting the progression of premalignant gastric lesions, which reiterates the need for intensified efforts through both eradication campaigns and ongoing surveillance to mitigate the GC burden. Furthermore, in this cohort, patients classified into the high-risk category based on the OLGA/OLGIM scores (stages III and IV), were approximately 20-fold more likely to progress to GC than patients with lower disease stages, although the OLGA/OLGIM staging system was applied retrospectively. This corroborates the findings from a previous meta-analysis (2018), which reported significantly elevated risk ratios for OLGA stages III/IV (RR 27.70 [95% CI 3.75–204.87]) vs. lower-risk stages.[86] Rugge et al.[101] performed a study in an Italian cohort of 1755 patients from a low-risk GC population and observed that OLGA staging is a reliable predictor of the risk of GC onset. In contrast, Lee et al.[88] investigated 2980 Singaporean patients and validated and recommended the use of the OLGIM score for GC surveillance in low-to-intermediate risk populations. Both cohorts reported a time to the first detection of neoplasia of <23 months, which suggests shorter follow-up intervals of 2 years for high-risk patients (OLGA/OLGIM stages III/IV). This recommendation differs from that of the European MAPS II guidelines, which suggest 3-year surveillance for patients with OLGA stages III–IV.

In a recent study, we reported the results of the Endoscopic Cohort and Histologic OLGA staging[102] study, which to date comprises 685 Chilean adults, a population at high risk of GC based on Sydney protocol biopsies. We observed significantly elevated HGD/GC rates, analyzed as a combined outcome, respected the OLGA and OLGIM classifications, with HR 14.8 (95% CI 1.8–1.25) and 34 (95% CI 4–286), respectively, in concordance with the results of the study reported by Rugge et al.[101] and Lee et al.[88] Notably, patients categorized into OLGA/OLGIM II stage showed no significantly increased risk of HGD/GC, contrary to the results reported by Lee et al.[88] Furthermore, our results indicate that OLGIM showed greater stability during follow-up compared with the OLGA system (62.0% vs. 47.0%), which is perhaps attributable to low inter-pathologist variability and is consistent with results reported by previous studies.[103] The higher HR and better interobserver agreement suggest that OLGIM may outperform OLGA as a GC risk assessment tool. Furthermore, although we detected one case of early-stage GC at 15 months, the median time to HGD/GA for OLGA/OLGIM stages III/IV was 33 months, which suggests that a 3-year surveillance interval, consistent with the recommendations of the European guidelines and international consensus statements,[9,104] is likely to be appropriate even in high-risk populations such as in Latin America. Recent guideline recommendations from a Chilean consensus for primary and secondary GC prevention recommend 3-year surveillance for OLGA stages III/IV and 5-year surveillance for OLGA stages I/II, based on our results.[21] Finally, 6 of the 7 cases of GC detected in the cohort were diagnosed during the early stages and resected endoscopically. This early detection rate is in contrast to that observed in the real-world scenario in our region where most GC cases are diagnosed during advanced stages and are associated with poor prognosis. These preliminary results suggest that endoscopic surveillance of high-risk GPNC may improve early detection of GC.

STRATEGIES AND GUIDELINES

Various strategies that incorporate recommendations for both primary and secondary prevention have emerged for early detection and management of GPNC and GC. Primary prevention strategies that recommend *H. pylori* testing during EGD, followed by appropriate treatment after detection are outlined in the European, Spanish, American, and Japanese[9,96-98,105] but not the Korean guidelines.[106] Although PG

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testing is useful to identify patients with advanced-stage GA, only the European guidelines recommend EGD after investigations reveal a low PGR, particularly in patients without *H. pylori* infection.[9] Japanese guidelines do not recommend use of PGI or PGII for population-based screening.[105]

Guidelines published by East Asian countries are aimed at early detection of GC and recommend EGD for all individuals aged ≥50 years in Japan[105] and for those aged between 40 and 74 years in Korea.[106] A 2-year interval between EGD screening is recommended in both countries,[105,107] without specific risk stratification for surveillance to promote an early-detection-and-resection approach. However, a study performed by Hamashima et al.[108] is underway in the Japanese population to determine whether extending the interval between EGD screening from 2- to 4-year intervals may benefit individuals at low risk of GC, which can potentially lead to a modification in their approach.

Table 1 shows the principal Western guidelines for GPMC surveillance. The British Society of Gastroenterology guidelines[96] recommend EGD screening in all individuals aged ≥50 years, particularly in those with known risk factors for GC such as male sex, smokers, patients with pernicious anemia, and in those with first-degree relatives diagnosed with GC. Additionally, endoscopic surveillance at 3-year intervals is recommended in patients with extensive CAG or IM or in specific cases with additional risk factors, including a strong family history of GC (defined as a first-degree relative or two or more second-degree relatives with GC) and persistent *H. pylori* infection. Similar recommendations are outlined by the MAPS-II European guidelines,[9] with a more frequent surveillance interval (every 1–2 years) in specific cases such as advanced-stage CAG and a family history of GC. Spanish guidelines[97] recommend EGD for patients aged ≥40 years or those who are 5 years older than the youngest affected relative in patients with a family history of GC. However, European guidelines define patients with OLGA/OLGIM stage III/IV scores as advanced-stage CAG and recommend EGD surveillance at 3-year intervals. However, Spanish guidelines recommend surveillance only in patients with extensive IM (OLGIM stages III/IV) with additional risk factors (incomplete-type lesions or a family history of GC) and discourage surveillance in patients with CAG without IM. British guidelines do not concur with the use of the OLGA or OLGIM classifications in regular practice but acknowledge their utility in research contexts.

The American Society for Gastrointestinal Endoscopy (ASGE) and the American Gastroenterological Association (AGA) do not provide recommendations for GC screening.[90,109] The ASGE guidelines are similar to the European guidelines with regard to surveillance recommendations only for patients with IM

Table 1. Principal Western guidelines for surveillance of gastric premalignant conditions

Recommendations	Chilean guideline	MAPS II (European guideline)	British guideline	AGA technical review	Spanish guideline
Year published	2014	2019	2019	2020–2021	2022
Atrophic gastritis surveillance	OLGA I–II 3 years OLGA III–IV 1 year	AG in antrum and corpus (OLGA III/IV): 3 years 1–2 years if first-degree family history of GC	3 years, only if extensive chronic AG or AG with additional risk factors	OLGA III/IV 3 years.	-
Intestinal metaplasia surveillance	OLGIM I–II 3 years OLGIM III–IV 1 year	IM only in antrum or corpus (if family history of GC, incomplete IM, AIG or persistent *Helicobacter pylori* infection) 3 years IM in both antrum and corpus 3 years 1–2 years if first-degree family history of GC	Extensive IM or IM with additional risk factors 3 years	Incomplete gastric IM, extensive gastric IM, family history of gastric cancer or immigrants from high incidence regions, surveillance may be considered in 3–5 years	OLGIM III–IV and incomplete IM or family history of GC 3 years
Low-grade dysplasia surveillance	1 year	1 year	1 year	-	1 year
High-grade dysplasia surveillance	6 months	6 months	6 months	-	6 months

AGA, American Gastroenterological Association; AG, atrophic gastritis; AIG, autoimmune gastritis; GC, gastric cancer; IM, intestinal metaplasia; MAPS, management of epithelial precancerous conditions and lesions in the stomach; OLGA, Operative Link for Gastritis Assessment; OLGIM, Operative Link for Gastric Intestinal Metaplasia Assessment.

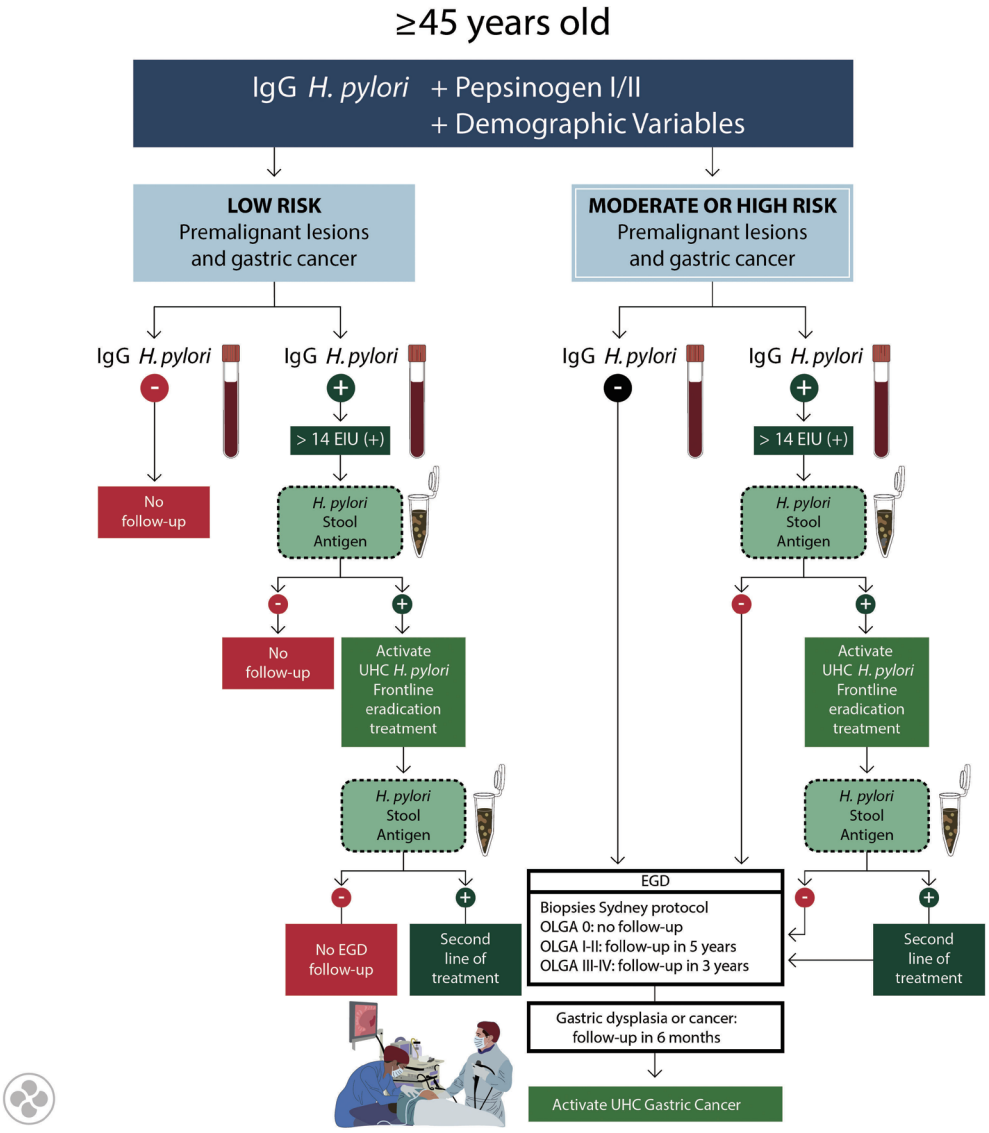

Fig. 5. Strategies for primary and secondary prevention of gastric cancer in asymptomatic individuals aged ≥45 years. EIU, enzime immunounits; UHC, universal health coverage; OLGA, Operative Link on Gastritis Assessment; EGD, esophagogastroduodenoscopy.

who present with risk factors; Asian heritage or a family history of GC are the only risk factors considered by these guidelines. However, the ASGE guidelines do not provide recommendations regarding optimal surveillance intervals or management strategies for CAG. In contrast, the AGA acknowledges the role of surveillance for advanced GA based on histopathological findings, anatomic distribution, and OLGA/OLGIM stages III/IV. With regard to IM, the AGA guidelines prioritize surveillance for patients with incomplete or extensive IM, a family history of GC, racial/ethnic minorities, or immigrants from high-incidence regions and recommend surveillance over 3- to 5-year intervals; however, the effects on the mortality risk remain unclear.[98]

The current guideline for GC in Chile recommends EGD in individuals aged ≥40 years with upper gastrointestinal symptoms such as epigastralgia that persists for >14 days.[7] However, in our recent study, we observed that although screening in patients aged 40 years appears to be appropriate, depending on symptom-based criteria for patient selection may not be the optimal approach,[110] which has prompted a shift toward implementation of screening strategies for the Chilean population. The National Association of Endoscopy of Chile recommends EGD for follow-up evaluation in patients aged >40 years diagnosed with GPMC, annual EGD in patients with extensive GA or OLGIM or OLGA stages III/IV, and EGD screening at 5-year intervals in those with intermediate-risk OLGA stages I/II or OLGA stage 0 with persistent *H. pylori* infection, potentially imposing a significant burden on health systems.[8]

A recent expert consensus in Chile[21] proposed preventive strategies for asymptomatic patients aged 35−44 years and ≥45 years. A combined approach using non-invasive tests was recommended for detection of *H. pylori*, followed by treatment for those with active infection in individuals aged 35−44 years. *H. pylori* antigen stool tests are recommended as a priority, and *H. pylori* IgG serology or blown air tests are suggested alternatives based on costs and implementation. A three-level approach is proposed for patients aged >45 years (Fig. 5). Level 1: patients undergo screening using *H. pylori*/PG I−II testing, considering individual baseline comorbidities to assess low- or intermediate-to-high GC risk. Level 2: *H. pylori* treatment is administered to those with positive results. Level 3: Patients undergo EGD together with the Sydney biopsy protocol in those with an intermediate-to-high GC risk, followed by OLGA assessment, performed after *H. pylori* treatment. Follow-up was defined for intermediate-to-high risk patients as 5-year surveillance intervals for patients with OLGA stage 0 and persistent *H. pylori* infection and patients with OLGA stages I−II and 3-year intervals for patients with OLGA stages III/IV. Surveillance is not recommended for patients with OLGA stage 0 without *H. pylori* infection. These risk assessments may be useful in other countries, particularly in Latin America to prioritize resource allocation for the population that needs them most.

An American group of experts recently published 13 recommendations for GC prevention and control[56] to address the lack of public health actions in Latin American countries. Among these recommendations, those directly associated with CAG and IM are significant, although all recommendations are useful. The recommendation to "Support development and dissemination of standard for quality care in GC prevention" emphasizes improved EGD quality, establishment of clear guidelines for biopsy collection, and consistency in reporting histopathological findings. Additionally, the recommendation to "Enable training of health care workforce specialized in GC" is important for better identification of patients with risk factors and provide more effective care. Notably, "Ensure endoscopic surveillance of patients with high-risk IM" aligns with the proposed Chilean consensus[21] and facilitates early intervention in gastric carcinogenesis.

CONCLUSIONS

Several geographical areas across Latin America show intermediate-to-high risk of GC; however, adequate prevention strategies are currently lacking. Although studies performed to investigate adequate surveillance based on histopathological scores have reported favorable results, further research that focuses on non-invasive and endoscopic classifications is warranted to determine their applicability within a regional context in the Chilean population. Considering the limited resources available for endoscopic screening, surveillance of patients with histopathologically documented high risk of GC appears to be a cost-effective approach in Latin America. Despite scarce resources, initiatives such as the Chilean consensus provide promising frameworks for comprehensive screening and surveillance based on primary and secondary prevention strategies.

Authors' Contribution

Conceptualization: all authors. Funding acquisition: Arnoldo Riquelme, Gonzalo Latorre. Project administration: Arnoldo Riquelme, Gonzalo Latorre. Supervision: Arnoldo Riquelme, Gonzalo Latorre. Writing—original draft: Felipe Silva. Writing—review & editing: all authors. Approval of final manuscript: all authors.

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REFERENCES

1. Sung H, Ferlay J, Siegel RL, et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 2021;71:209-249.
2. de Salud M. Cancer Surveillance Report. Mortality Analysis. Decade 2009-2018. Chile 2020 [accessed on February 22, 2024]. Available from: http://epi.minsal.cl/wp-content/uploads/2021/05/Informe_Mortalidad_por_Cancer_2009_2018.pdf.
3. Correa P. A human model of gastric carcinogenesis. Cancer Res 1988;48:3554-3560.
4. IARC Working Group on the Evaluation of Carcinogenic Risks to Humans. Schistosomes, Liver Flukes and *Helicobacter pylori*. Lyon (FR): International Agency for Research on Cancer, 1994.
5. Allum WH, Powell DJ, McConkey CC, Fielding JW. Gastric cancer: a 25-year review. Br J Surg 1989;76:535-540.
6. Smyth EC, Nilsson M, Grabsch HI, van Grieken NC, Lordick F. Gastric cancer. Lancet 2020;396:635-648.
7. de Salud M. AUGE clinical guideline on gastric cancer, 2014 [accessed on February 22, 2024]. Available from: https://www.minsal.cl/sites/default/files/files/GPC%20G%C3%A1strico%20(PL).pdf.
8. Rollán A, Cortés P, Calvo A, et al. [Recommendations of the Chilean association for digestive endoscopy for the management of gastric pre-malignant lesions]. Rev Med Chil 2014;142:1181-1192. Spanish
9. Pimentel-Nunes P, Libânio D, Marcos-Pinto R, et al. Management of epithelial precancerous conditions and lesions in the stomach (MAPS II): European Society of Gastrointestinal Endoscopy (ESGE), European *Helicobacter* and Microbiota Study Group (EHMSG), European Society of Pathology (ESP), and Sociedade Portuguesa de Endoscopia Digestiva (SPED) guideline update 2019. Endoscopy 2019;51:365-388.
10. Latorre SG, Álvarez OJ, Ivanovic-Zuvic SD, et al. [Coverage of diagnostic upper gastrointestinal endoscopy for the prevention of gastric cancer in Chile: results from the 2009-2010 national health survey]. Rev Med Chil 2015;143:1198-1205. Spanish
11. Chiu PWY, Uedo N, Singh R, et al. An Asian consensus on standards of diagnostic upper endoscopy for neoplasia. Gut 2019;68:186-197.

12. Miura Y, Osawa H, Sugano K. Recent progress of image-enhanced endoscopy for upper gastrointestinal neoplasia and associated lesions. Dig Dis 2024;42:186-198.
13. Desai M, Boregowda U, Srinivasan S, et al. Narrow band imaging for detection of gastric intestinal metaplasia and dysplasia: a systematic review and meta-analysis. J Gastroenterol Hepatol 2021;36:2038-2046.
14. Kimura K, Takemoto T. An endoscopic recognition of the atrophic border and its significance in chronic gastritis. Endoscopy 1969;1:87-97.
15. Masuyama H, Yoshitake N, Sasai T, et al. Relationship between the degree of endoscopic atrophy of the gastric mucosa and carcinogenic risk. Digestion 2015;91:30-36.
16. Pimentel-Nunes P, Libânio D, Lage J, et al. A multicenter prospective study of the real-time use of narrow-band imaging in the diagnosis of premalignant gastric conditions and lesions. Endoscopy 2016;48:723-730.
17. Esposito G, Pimentel-Nunes P, Angeletti S, et al. Endoscopic grading of gastric intestinal metaplasia (EGGIM): a multicenter validation study. Endoscopy 2019;51:515-521.
18. Latorre G, Vargas JI, Shah SC, et al. Implementation of the updated Sydney system biopsy protocol improves the diagnostic yield of gastric preneoplastic conditions: results from a real-world study. Gastroenterol Hepatol 2023 Aug 19 [Epub]. https://doi.org/10.1016/j.gastrohep.2023.08.005.
19. Rugge M, Genta RM; OLGA Group. Staging gastritis: an international proposal. Gastroenterology 2005;129:1807-1808.
20. Capelle LG, de Vries AC, Haringsma J, et al. The staging of gastritis with the OLGA system by using intestinal metaplasia as an accurate alternative for atrophic gastritis. Gastrointest Endosc 2010;71:1150-1158.
21. Corsi Sotelo Ó, Pizarro Rojas M, Rollán Rodríguez A, et al. Chilean consensus by expert panel using the Delphi technique for primary and secondary prevention of gastric cancer. Gastroenterol Hepatol 2024 Feb 2 [Epub]. https://doi.org/10.1016/j.gastrohep.2024.01.008.
22. Ilic M, Ilic I. Epidemiology of stomach cancer. World J Gastroenterol 2022;28:1187-1203.
23. Ferlay J, Colombet M, Soerjomataram I, et al. Cancer statistics for the year 2020: an overview. Int J Cancer 2021;149:778-789.
24. Anderson WF, Rabkin CS, Turner N, Fraumeni JF Jr, Rosenberg PS, Camargo MC. The changing face of noncardia gastric cancer incidence among US non-Hispanic whites. J Natl Cancer Inst 2018;110:608-615.
25. Arnold M, Park JY, Camargo MC, Lunet N, Forman D, Soerjomataram I. Is gastric cancer becoming a rare disease? A global assessment of predicted incidence trends to 2035. Gut 2020;69:823-829.
26. Rugge M, Genta RM, Di Mario F, et al. Gastric cancer as preventable disease. Clin Gastroenterol Hepatol 2017;15:1833-1843.
27. Coati I, Fassan M, Farinati F, Graham DY, Genta RM, Rugge M. Autoimmune gastritis: pathologist's viewpoint. World J Gastroenterol 2015;21:12179-12189.
28. Correa P, Piazuelo MB. The gastric precancerous cascade. J Dig Dis 2012;13:2-9.
29. Correa P, Houghton J. Carcinogenesis of *Helicobacter pylori*. Gastroenterology 2007;133:659-672.
30. Chiang TH, Chang WJ, Chen SL, et al. Mass eradication of *Helicobacter pylori* to reduce gastric cancer incidence and mortality: a long-term cohort study on Matsu Islands. Gut 2021;70:243-250.
31. Li Y, Choi H, Leung K, Jiang F, Graham DY, Leung WK. Global prevalence of *Helicobacter pylori* infection between 1980 and 2022: a systematic review and meta-analysis. Lancet Gastroenterol Hepatol 2023;8:553-564.
32. Hooi JKY, Lai WY, Ng WK, et al. Global prevalence of *Helicobacter pylori* infection: systematic review and meta-analysis. Gastroenterology 2017;153:420-429.
33. Ferreccio C, Rollán A, Harris PR, et al. Gastric cancer is related to early *Helicobacter pylori* infection in a high-prevalence country. Cancer Epidemiol Biomarkers Prev 2007;16:662-667.
34. Silva F, Latorre G, Medel P, et al. [Reduction in *Helicobacter pylori* infection among patients referred for upper gastrointestinal endoscopy in Santiago, Chile, between 2010-2020]. Rev Gastroenterol Peru 2024;44:14-20. Spanish
35. Correa P, Piazuelo MB. *Helicobacter pylori* infection and gastric adenocarcinoma. US Gastroenterol Hepatol Rev 2011;7:59-64.
36. Correa P, Haenszel W, Cuello C, Tannenbaum S, Archer M. A model for gastric cancer epidemiology. Lancet 1975;306:58-60.
37. Kumar S, Patel GK, Ghoshal UC. *Helicobacter pylori*-induced inflammation: possible factors modulating the risk of gastric cancer. Pathogens 2021;10:1099.
38. Zhang L, Liu Y, You P, Feng G. Occurrence of gastric cancer in patients with atrophic gastritis during long-term follow-up. Scand J Gastroenterol 2018;53:843-848.
39. Gawron AJ, Shah SC, Altayar O, et al. AGA technical review on gastric intestinal metaplasia-natural history and clinical outcomes. Gastroenterology 2020;158:705-731.e5.
40. de Vries AC, van Grieken NC, Looman CW, et al. Gastric cancer risk in patients with premalignant gastric lesions: a nationwide cohort study in the Netherlands. Gastroenterology 2008;134:945-952.
41. Khazaaleh S, Alomari M, Rashid MU, Castaneda D, Castro FJ. Gastric intestinal metaplasia and gastric cancer prevention: watchful waiting. Cleve Clin J Med 2024;91:33-39.
42. Tava F, Luinetti O, Ghigna MR, et al. Type or extension of intestinal metaplasia and immature/atypical "indefinite-for-dysplasia" lesions as predictors of gastric neoplasia. Hum Pathol 2006;37:1489-1497.
43. Tosi P, Filipe MI, Luzi P, et al. Gastric intestinal metaplasia type III cases are classified as low-grade dysplasia on the basis of morphometry. J Pathol 1993;169:73-78.
44. Dixon MF. Gastrointestinal epithelial neoplasia: Vienna revisited. Gut 2002;51:130-131.
45. Huang YK, Yu JC, Kang WM, et al. Significance of serum pepsinogens as a biomarker for gastric cancer and atrophic gastritis screening: a systematic review and meta-analysis. PLoS One 2015;10:e0142080.
46. Mansour-Ghanaei F, Joukar F, Baghaee M, Sepehrimanesh M, Hojati A. Only serum pepsinogen I and pepsinogen I/II ratio are specific and sensitive biomarkers for screening of gastric cancer. Biomol Concepts 2019;10:82-90.
47. Miki K, Urita Y. Using serum pepsinogens wisely in a clinical practice. J Dig Dis 2007;8:8-14.
48. Samloff IM. Cellular localization of group I pepsinogens in human gastric mucosa by immunofluorescence. Gastroenterology 1971;61:185-188.
49. Samloff IM, Liebman WM. Cellular localization of the group II pepsinogens in human stomach and duodenum by immunofluorescence. Gastroenterology 1973;65:36-42.
50. Boubrik F, Belmouden A, El Kadmiri N. Potential non-invasive biomarkers of *Helicobacter pylori*-associated gastric cancer. J Gastrointest Cancer 2022;53:1113-1120.
51. Cai Q, Zhu C, Yuan Y, et al. Development and validation of a prediction rule for estimating gastric cancer risk in the Chinese high-risk population: a nationwide multicentre study. Gut 2019;68:1576-1587.
52. Tu H, Sun L, Dong X, et al. A serological biopsy using five stomach-specific circulating biomarkers for gastric cancer risk assessment: a multi-phase study. Am J Gastroenterol 2017;112:704-715.
53. Syrjänen K. Accuracy of Serum Biomarker Panel (GastroPanel®) in the diagnosis of atrophic gastritis of the corpus. Systematic review

and meta-analysis. Anticancer Res 2022;42:1679-1696.
54. Latorre G, Pizarro M, Ford JS, et al. Evaluation of trefoil factor 3 as a non-invasive biomarker of gastric intestinal metaplasia and gastric cancer in a high-risk population. Gastroenterol Hepatol 2023;46:411-418.
55. Zhu XL, Ren LF, Wang HP, et al. Plasma microRNAs as potential new biomarkers for early detection of early gastric cancer. World J Gastroenterol 2019;25:1580-1591.
56. Riquelme A, Abnet CC, Goodman KJ, et al. Recommendations for gastric cancer prevention and control in the Americas. Lancet Reg Health Am 2023;27:100608.
57. Hamashima C, Ogoshi K, Narisawa R, et al. Impact of endoscopic screening on mortality reduction from gastric cancer. World J Gastroenterol 2015;21:2460-2466.
58. Yalamarthi S, Witherspoon P, McCole D, Auld CD. Missed diagnoses in patients with upper gastrointestinal cancers. Endoscopy 2004;36:874-879.
59. Pimenta-Melo AR, Monteiro-Soares M, Libânio D, Dinis-Ribeiro M. Missing rate for gastric cancer during upper gastrointestinal endoscopy: a systematic review and meta-analysis. Eur J Gastroenterol Hepatol 2016;28:1041-1049.
60. Kim SY, Park JM. Quality indicators in esophagogastroduodenoscopy. Clin Endosc 2022;55:319-331.
61. Teh JL, Tan JR, Lau LJ, et al. Longer examination time improves detection of gastric cancer during diagnostic upper gastrointestinal endoscopy. Clin Gastroenterol Hepatol 2015;13:480-487.e2.
62. Ferrari C, Tadros M. Enhancing the quality of upper gastrointestinal endoscopy: current indicators and future trends. Gastroenterol Insights 2023;15:1-18.
63. Bisschops R, Areia M, Coron E, et al. Performance measures for upper gastrointestinal endoscopy: a European Society of Gastrointestinal Endoscopy (ESGE) quality improvement initiative. Endoscopy 2016;48:843-864.
64. Khan R, Gimpaya N, Vargas JI, et al. The Toronto upper gastrointestinal cleaning score: a prospective validation study. Endoscopy 2023;55:121-128.
65. Gotoda T, Uedo N, Yoshinaga S, et al. Basic principles and practice of gastric cancer screening using high-definition white-light gastroscopy: eyes can only see what the brain knows. Dig Endosc 2016;28(Suppl 1):2-15.
66. Li J, Wang L, Hu W, et al. Effect of premedication with pronase before upper gastrointestinal endoscopy: a multicenter prospective randomized controlled study. J Clin Gastroenterol 2024;58:53-56.
67. Kuo CH, Sheu BS, Kao AW, Wu CH, Chuang CH. A defoaming agent should be used with pronase premedication to improve visibility in upper gastrointestinal endoscopy. Endoscopy 2002;34:531-534.
68. Monrroy H, Vargas JI, Glasinovic E, et al. Use of N-acetylcysteine plus simethicone to improve mucosal visibility during upper GI endoscopy: a double-blind, randomized controlled trial. Gastrointest Endosc 2018;87:986-993.
69. Cai MX, Gao Y, Li L, et al. Four-hour fasting for semifluids and 2-hour fasting for water improves the patient experience of esophagogastroduodenoscopy: a randomized controlled trial. Gut Liver 2023;17:382-388.
70. Eshmuratov A, Nah JC, Kim N, et al. The correlation of endoscopic and histological diagnosis of gastric atrophy. Dig Dis Sci 2010;55:1364-1375.
71. Redéen S, Petersson F, Jönsson KA, Borch K. Relationship of gastroscopic features to histological findings in gastritis and *Helicobacter pylori* infection in a general population sample. Endoscopy 2003;35:946-950.
72. Zhao Z, Yin Z, Wang S, et al. Meta-analysis: the diagnostic efficacy of chromoendoscopy for early gastric cancer and premalignant gastric lesions. J Gastroenterol Hepatol 2016;31:1539-1545.
73. Sinonquel P, Vermeire S, Maes F, Bisschops R. Advanced imaging in gastrointestinal endoscopy: a literature review of the current state of the art. GE Port J Gastroenterol 2023;30:175-191.
74. van der Sommen F, Curvers WL, Nagengast WB. Novel developments in endoscopic mucosal imaging. Gastroenterology 2018;154:1876-1886.
75. Martins BC, Moura RN, Kum AST, Matsubayashi CO, Marques SB, Safatle-Ribeiro AV. Endoscopic imaging for the diagnosis of neoplastic and pre-neoplastic conditions of the stomach. Cancers (Basel) 2023;15:2445.
76. Yashima K, Onoyama T, Kurumi H, et al. Current status and future perspective of linked color imaging for gastric cancer screening: a literature review. J Gastroenterol 2023;58:1-13.
77. Zhou J, Wu H, Fan C, Chen S, Liu A. Comparison of the diagnostic efficacy of blue laser imaging with narrow band imaging for gastric cancer and precancerous lesions: a meta-analysis. Rev Esp Enferm Dig 2020;112:649-658.
78. Xu M, Zhou W, Wu L, et al. Artificial intelligence in the diagnosis of gastric precancerous conditions by image-enhanced endoscopy: a multicenter, diagnostic study (with video). Gastrointest Endosc 2021;94:540-548.e4.
79. Zhao Q, Chi T. Deep learning model can improve the diagnosis rate of endoscopic chronic atrophic gastritis: a prospective cohort study. BMC Gastroenterol 2022;22:133.
80. Mu G, Zhu Y, Niu Z, et al. Expert-level classification of gastritis by endoscopy using deep learning: a multicenter diagnostic trial. Endosc Int Open 2021;9:E955-E964.
81. Tao X, Zhu Y, Dong Z, et al. An artificial intelligence system for chronic atrophic gastritis diagnosis and risk stratification under white light endoscopy. Dig Liver Dis 2024;56:1319-1326.
82. Yagi K, Nakamura A, Sekine A. Comparison between magnifying endoscopy and histological, culture and urease test findings from the gastric mucosa of the corpus. Endoscopy 2002;34:376-381.
83. Yagi K, Watanabe J, Nakamura A, Sekine A. Magnifying views of gastritis-AB classification. Stomach Intestine 2007;42:697-704.
84. Tahara T, Shibata T, Nakamura M, et al. Gastric mucosal pattern by using magnifying narrow-band imaging endoscopy clearly distinguishes histological and serological severity of chronic gastritis. Gastrointest Endosc 2009;70:246-253.
85. Yoo CH, Park MI, Park SJ, et al. Observer variability in gastric neoplasm assessment using the vessel plus surface classification for magnifying endoscopy with narrow band imaging. Clin Endosc 2014;47:74-78.
86. Yue H, Shan L, Bin L. The significance of OLGA and OLGIM staging systems in the risk assessment of gastric cancer: a systematic review and meta-analysis. Gastric Cancer 2018;21:579-587.
87. Rugge M, Genta RM, Fassan M, et al. OLGA gastritis staging for the prediction of gastric cancer risk: a long-term follow-up study of 7436 patients. Am J Gastroenterol 2018;113:1621-1628.
88. Lee JWJ, Zhu F, Srivastava S, et al. Severity of gastric intestinal metaplasia predicts the risk of gastric cancer: a prospective multicentre cohort study (GCEP). Gut 2022;71:854-863.
89. El-Zimaity HM, Graham DY. Evaluation of gastric mucosal biopsy site and number for identification of *Helicobacter pylori* or intestinal metaplasia: role of the Sydney system. Hum Pathol 1999;30:72-77.
90. Shah SC, Piazuelo MB, Kuipers EJ, Li D. AGA clinical practice update on the diagnosis and management of atrophic gastritis: expert review. Gastroenterology 2021;161:1325-1332.e7.
91. Maric L, Castaneda D, Singh H, Bejarano P, Jimenez Cantisano B, Castro FJ. Kimura-Takemoto classification: a tool to predict gastric intestinal metaplasia progression to advanced gastric neoplasia. Dig Dis Sci 2022;67:4092-4099.
92. Chen M, Liu XL, Zhu XJ, et al. Endoscopic grading of gastric atro-

phy and histological gastritis staging on risk assessment for early gastric cancer: a case-control study. J Dig Dis 2023;24:262-270.
93. Shichijo S, Hirata Y, Niikura R, et al. Histologic intestinal metaplasia and endoscopic atrophy are predictors of gastric cancer development after *Helicobacter pylori* eradication. Gastrointest Endosc 2016;84:618-624.
94. Pimentel-Nunes P, Dobru D, Libânio D, Dinis-Ribeiro M. White flat lesions in the gastric corpus may be intestinal metaplasia. Endoscopy 2017;49:617-618.
95. Fang S, Fu Y, Du S, et al. The role of the endoscopic grading of gastric intestinal metaplasia in assessing gastric cancer risk: a systematic review and meta-analysis. Front Oncol 2022;12:1018248.
96. Banks M, Graham D, Jansen M, et al. British Society of Gastroenterology guidelines on the diagnosis and management of patients at risk of gastric adenocarcinoma. Gut 2019;68:1545-1575.
97. Cubiella J, Pérez Aisa Á, Cuatrecasas M, et al. Gastric cancer screening in low incidence populations: position statement of AEG, SEED and SEAP. Gastroenterol Hepatol 2021;44:67-86.
98. Gupta S, Li D, El Serag HB, et al. AGA clinical practice guidelines on management of gastric intestinal metaplasia. Gastroenterology 2020;158:693-702.
99. Du S, Yang Y, Fang S, et al. Gastric cancer risk of intestinal metaplasia subtypes: a systematic review and meta-analysis of cohort studies. Clin Transl Gastroenterol 2021;12:e00402.
100. Piazuelo MB, Bravo LE, Mera RM, et al. The Colombian chemoprevention trial: 20-year follow-up of a cohort of patients with gastric precancerous lesions. Gastroenterology 2021;160:1106-1117.e3.
101. Rugge M, Meggio A, Pravadelli C, et al. Gastritis staging in the endoscopic follow-up for the secondary prevention of gastric cancer: a 5-year prospective study of 1755 patients. Gut 2019;68:11-17.
102. Latorre G, Silva F, Montero I, et al. Comparison of OLGA and OLGIM as predictors of gastric cancer in a Latin American population: the ECHOS study. Gut 2023 Dec 26 [Epub]. https://doi.org/10.1136/gutjnl-2023-331059.
103. Isajevs S, Liepniece-Karele I, Janciauskas D, et al. Gastritis staging: interobserver agreement by applying OLGA and OLGIM systems. Virchows Arch 2014;464:403-407.
104. Rugge M, Genta RM, Malfertheiner P, et al. RE.GA.IN.: the real-world gastritis initiative–updating the updates. Gut 2024;73:407-441.
105. Hamashima C; Systematic Review Group and Guideline Development Group for Gastric Cancer Screening Guidelines. Update version of the Japanese guidelines for gastric cancer screening. Jpn J Clin Oncol 2018;48:673-683.
106. Park HA, Nam SY, Lee SK, et al. The Korean guideline for gastric cancer screening. J Korean Med Assoc 2015;58:373-384.
107. Hamashima C. Cancer screening guidelines and policy making: 15 years of experience in cancer screening guideline development in Japan. Jpn J Clin Oncol 2018;48:278-286.
108. Hamashima C, Yoshimura K, Fukao A. A study protocol for expanding the screening interval of endoscopic screening for gastric cancer based on individual risks: prospective cohort study of gastric cancer screening. Ann Transl Med 2020;8:1604.
109. Evans JA, Chandrasekhara V, Chathadi KV, et al. The role of endoscopy in the management of premalignant and malignant conditions of the stomach. Gastrointest Endosc 2015;82:1-8.
110. Silva F, Bustamante M, Latorre G, et al. Diagnosis of gastric premalignant conditions according to age and symptoms: results from a Chilean cohort study. Gastroenterol Latinoam 2023;34:209.
111. Miwata T, Quach DT, Hiyama T, et al. Interobserver and intraobserver agreement for gastric mucosa atrophy. BMC Gastroenterol 2015;15:95.