

Review Article

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Gastric Cancer Today: Epidemiology and Treatment-An Updated Review

Ana Paula Mendes^{1*}, Fernando de Oliveira Dutra², Ian Caldeira Ruppen¹, André Cesar Leandro¹, Larissa da Rosa Piccoli¹, Tauane Cano Barreto¹, Emily Eduarda Hellmann¹, Priscila De Oliveira Barros¹, Camilla Antunes Zanini³, Sarila Hali Kloster Lopes¹, Lara Beatriz Dallaqua Bitiati¹, Bruno Tadim Carderelli⁴, Henrique Marques Dagostin⁵, Maria Clara Costa Calvo¹, Ana Carolina Langendyk Rodrigues¹

¹Centro Universitario Inga Uninga, Maringa, PR, Brazil

²Hospital Memorial Uninga HMU, Maringa, PR, Brazil

³Faculdade Morgana Potrich, Mineiros, GO, Brazil

⁴Faculdade Cesumar Unicesumar, Maringa, PR Brazil

⁵Universidade Federal Rural do Semi Arido Ufersa Mossoro RN, Brazil

ABSTRACT

Gastric cancer remains a serious public health challenge, ranking as the fifth most incident malignancy and the fourth leading cause of cancer related death worldwide. Current epidemiology shows marked regional variation, with high rates in East Asia, Eastern Europe, and South America, while incidence has been declining in most highincome countries an effect attributed to Helicobacter pylori control, improvements in food refrigeration, and reduced smoking rates. In Brazil, the estimated incidence for 2023 to 2025 is 13.44 cases per 100,000 men and 7.31 per 100,000 women. Curative treatment is based on radical gastrectomy with D2 lymphadenectomy, complemented by perioperative chemotherapy with the FLOT regimen, which has demonstrated a survival benefit. In metastatic disease, the advent of immunotherapy has reshaped the landscape: nivolumab combined with chemotherapy has shown superior overall survival compared to chemotherapy alone, and the addition of pembrolizumab to trastuzumab has become the new standard for HER2 positive tumors. Moreover, the molecular classification proposed by ESMO now guides targeted therapies, including FGFR2b and Claudin 18.2 inhibitors. Despite these advances, five year survival remains below 40 % globally, underscoring the need for high risk screening programs, primary prevention policies, and equitable access to high complexity centers.

*Corresponding author

Ian Caldeira Ruppen, Centro Universitaario Inga Uninga, Maringa, Parana, Brazil.

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Introduction

Gastric cancer (GC) imposes a tremendous global burden of morbidity and mortality, accounting for approximately 1 million new cases and 770,000 deaths in 2024 [1]. Despite diagnostic and therapeutic advances, lethality remains high especially in low and middle income countries, where most diagnoses occur at advanced stages. Historically linked to Helicobacter pylori infection, GC has a multifactorial etiology that includes diets high in salt and nitrites, tobacco and alcohol consumption, obesity, and genetic predispositions such as CDH1 mutations and gastric polyposis syndromes [2]. Modern epidemiology reveals a shift in predominant histological subtype, with a gradual rise in cardia adenocarcinomas at the expense of non-cardia tumors possibly related to gastroesophageal reflux disease and obesity [3].

Emerging trends of early onset GC (< 50 years) also raise concern and suggest environmental exposures and microbiome alterations as contributing factors [4]. Population based screening policies

such as Japan's and Korea's biennial endoscopy programs have significantly reduced mortality, highlighting the importance of early detection [5]. In Brazil, however, universal screening is not recommended; efforts focus on gastric atrophy surveillance and H. pylorieradication [6]. Concurrently, molecular insights have advanced with the TCGA classification, which delineates four subtypes (EBV positive, MSI, genomically stable, and chromosomal instability), enabling targeted therapies and immunotherapeutic selection [7]. Overall, understanding GC's evolving epidemiology and biology is imperative for designing prevention, diagnostic, and treatment strategies capable of improving prognosis in this devastating disease.

Objectives

This review examines the current epidemiology, risk factors, and therapeutic approaches in gastric cancer, emphasizing recent evidence and future perspectives.

Materials and Methods

A literature review was conducted using the PubMed, SCIELO, Google Scholar, and ScienceDirect databases, focusing on publications from 2017 to early 2025.

Discussion

Modern GC management requires a multidisciplinary approach guided by precise staging via computed tomography, endoscopic ultrasound, and when indicated diagnostic laparoscopy. For T2–T4a/N+ disease, perioperative chemotherapy with FLOT (fluorouracil, leucovorin, oxaliplatin, and docetaxel) has become the standard, demonstrating a 9 % absolute improvement in five year overall survival compared to ECX (epirubicin, cisplatin, and capecitabine). Patients ineligible for FLOT may receive CROSS based or platinum based chemoradiotherapy [8]. Radical gastrectomy with D2 lymphadenectomy remains fundamental, though minimally invasive techniques offer lower morbidity without compromising oncologic outcomes in experienced centers [9].

In the metastatic setting, immunotherapy has revolutionized treatment. The CheckMate 649 trial showed that nivolumab plus fluoropyrimidine platinum chemotherapy increased median overall survival to 14.3 months versus 10.3 months for chemotherapy alone, with the greatest benefit in PD L1 CPS ≥ 5 tumors [10,11]. In HER2 positive disease, KEYNOTE 811 demonstrated a 74 % response rate and a 22 % reduction in mortality risk with pembrolizumab, trastuzumab, and chemotherapy, establishing a new first line paradigm [12]. Recently approved targeted agents include the bispecific antibody zanidatamab (HER2/HER2) and the anti Claudin 18.2 monoclonal antibody zolbetuximab, both showing promising phase III results. Therapeutic decisions must also consider microsatellite status and genomic instability: MSI high tumors exhibit up to a 60 % response rate to PD 1 inhibitors in the first line, potentially obviating cytotoxic chemotherapy [7].

Maintenance strategies such as trifluridine/tipiracil or ramucirumab plus paclitaxel are options after platinum failure, though quality of life benefits remain modest [2]. From a public health perspective, H. pylori eradication policies are cost effective and can reduce non cardia GC incidence by up to 40 % [5]. Nutritional interventions such as increased intake of fruits and vegetables and reduced consumption of processed foods also confer consistent benefits, though selenium and vitamin C supplementation remain controversial. Persistent disparities in access to endoscopic diagnosis and referral centers perpetuate high mortality rates across Latin America [6,13-15].

Conclusion

Advances in the epidemiology and molecular biology of gastric cancer have transformed diagnostic and therapeutic paradigms in the twenty first century. While global incidence is declining, heterogeneous regional patterns and rising early onset cases present ongoing challenges. Robust evidence supports H. pylori eradication and targeted endoscopic screening in high risk populations as effective secondary prevention strategies. Therapeutically, modern perioperative chemotherapy combined with high quality surgery improves cure rates in locally advanced disease; meanwhile, in metastatic GC, the integration of immunotherapy and molecularly driven targeted agents redefines prognosis. Yet equitable access to early diagnosis, biomarker testing, and high cost treatments remains the principal barrier to fully realizing these innovations particularly in middle income countries like Brazil.

Future research should prioritize predictive biomarkers of response, rational combinations of immune checkpoint inhibitors, de escalation strategies following pathological complete response, and primary prevention approaches addressing diet, microbiota, and emerging environmental exposures. Patient navigation programs and telemedicine may help mitigate geographic obstacles and optimize care pathways. Overcoming gastric cancer demands the integration

of basic science, rigorous clinical trials, and focused public health policies to ensure that recent advances translate into longer survival and improved quality of life for all affected patients.

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