Cardia Insufficiency as a Component of Gastroesophageal Reflux Disease and a Factor in Esophageal Carcinogenesis

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ABSTRACT

Gastroesophageal reflux disease (GERD) is among the most common gastrointestinal disorders and represents an important risk factor for esophageal adenocarcinoma [4,8]. Dysfunction of the lower esophageal sphincter (cardia insufficiency) plays a central role in its development. Long-term exposure of the esophageal mucosa to gastric acid and bile acids leads to chronic inflammation, oxidative stress, and accumulation of genetic alterations, which may ultimately result in malignant transformation [7,12]. This paper reviews current data on the sequence of morphological changes, molecular mechanisms of carcinogenesis, and clinical implications for surveillance.

Keywords: GERD, lower esophageal sphincter, Barrett's esophagus, carcinogenesis, adenocarcinoma

Introduction

Gastroesophageal reflux disease is a chronic condition characterized by repeated reflux of gastric contents into the esophagus, leading to mucosal damage. Epidemiological studies estimate that GERD affects up to one-fifth of the adult population worldwide [4,8].

Particular concern is associated with its long-term complications, especially esophageal adenocarcinoma, which has demonstrated a steady increase in incidence over recent decades [8,13]. Although relatively uncommon, this malignancy is associated with a poor prognosis and high mortality.

At the core of GERD pathogenesis lies dysfunction of the lower esophageal sphincter. When this barrier loses its competence, reflux episodes become more frequent and prolonged, exposing the esophageal epithelium to aggressive chemical factors.

The present work aims to summarize current evidence on the role of cardia insufficiency in GERD and its contribution to esophageal carcinogenesis.

Methods

A narrative review design was used. Relevant studies were retrieved from PubMed and Scopus databases.

Selection criteria included:

- publications with clinical or experimental relevance
- widely cited studies and international guidelines
- articles addressing GERD, Barrett's esophagus, and carcinogenesis

The analysis was based on comparison and synthesis of available data rather than formal meta-analysis.

Results

Pathophysiological Basis

The lower esophageal sphincter serves as the main barrier preventing reflux. In conditions of insufficiency, its basal tone decreases, transient relaxations become more frequent, and esophageal clearance is impaired (figure1).

As a result, the mucosa is repeatedly exposed to acidic and biliary contents, which have a damaging effect over time.

Figure 1. Pathogenesis of GERD and esophageal carcinogenesis

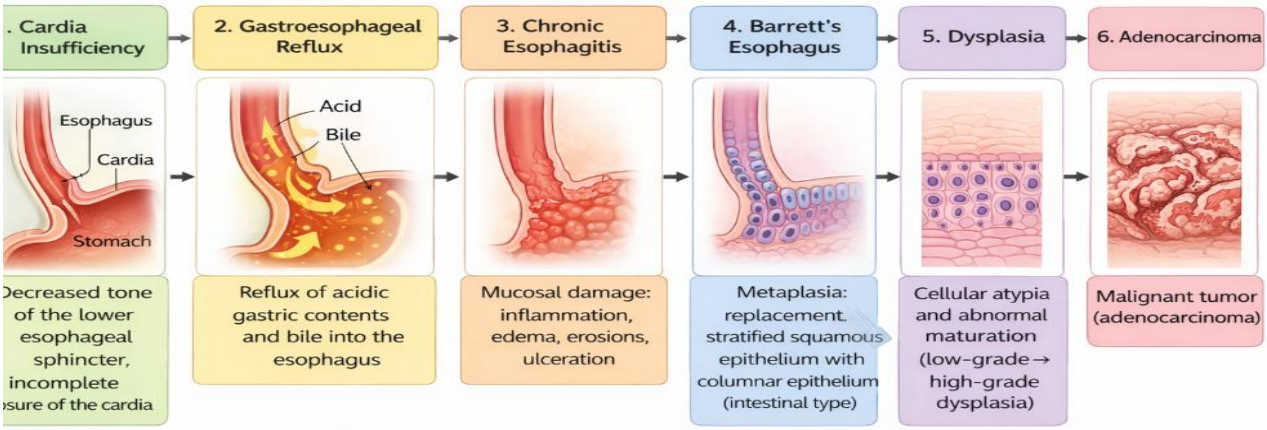

Figure 1. Pathogenesis of GERD and esophageal carcinogenesis.

Morphological Sequence

The progression of structural changes follows a well-recognized pattern:

Cardia insufficiency → reflux → chronic esophagitis → Barrett's esophagus → dysplasia → adenocarcinoma (figure1)

Initially, reflux induces inflammation of the squamous epithelium. With persistent injury, the epithelium undergoes metaplastic transformation into columnar epithelium containing goblet cells, known as Barrett's esophagus [1,2,10].

Further progression involves dysplastic changes, with a markedly increased risk of malignant transformation in high-grade dysplasia [15].

Molecular Mechanisms

At the molecular level, carcinogenesis is associated with progressive accumulation of genetic damage. Among the most important alterations are:

- mutations in tumor suppressor genes (notably p53)
- chromosomal instability
- epigenetic dysregulation
- impaired apoptosis

Chronic exposure to refluxate induces oxidative stress, which in turn leads to DNA damage and activation of oncogenic pathways [7,12] (figure2).

In addition, bile acids have been shown to promote intestinal-type differentiation through activation of CDX2 expression [6].

Figure 2. Molecular mechanisms of esophageal carcinogenesis

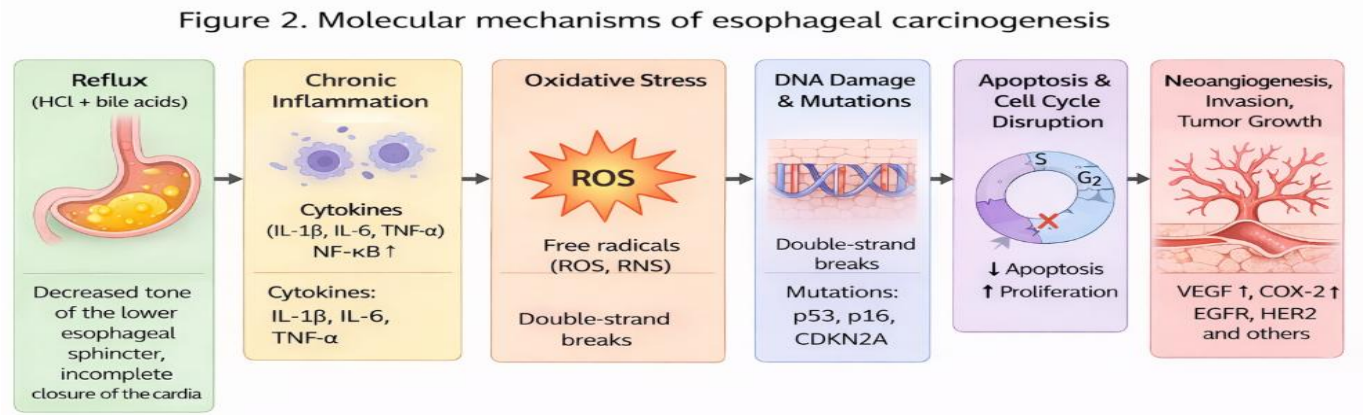

Figure 2. Molecular mechanisms of esophageal carcinogenesis.

Chronic acid-bile exposure induces oxidative stress, DNA damage, p53 mutations, and disruption of apoptosis, leading to uncontrolled cell proliferation.

Risk Factors

Several conditions exacerbate LES dysfunction and increase the severity of reflux (figure 3):

- abdominal obesity, which increases intra-abdominal pressure

- hiatal hernia, which disrupts anatomical integrity of the sphincter mechanism
- frequent reflux episodes (at least once weekly)

These factors contribute not only to symptom severity but also to long-term complications.

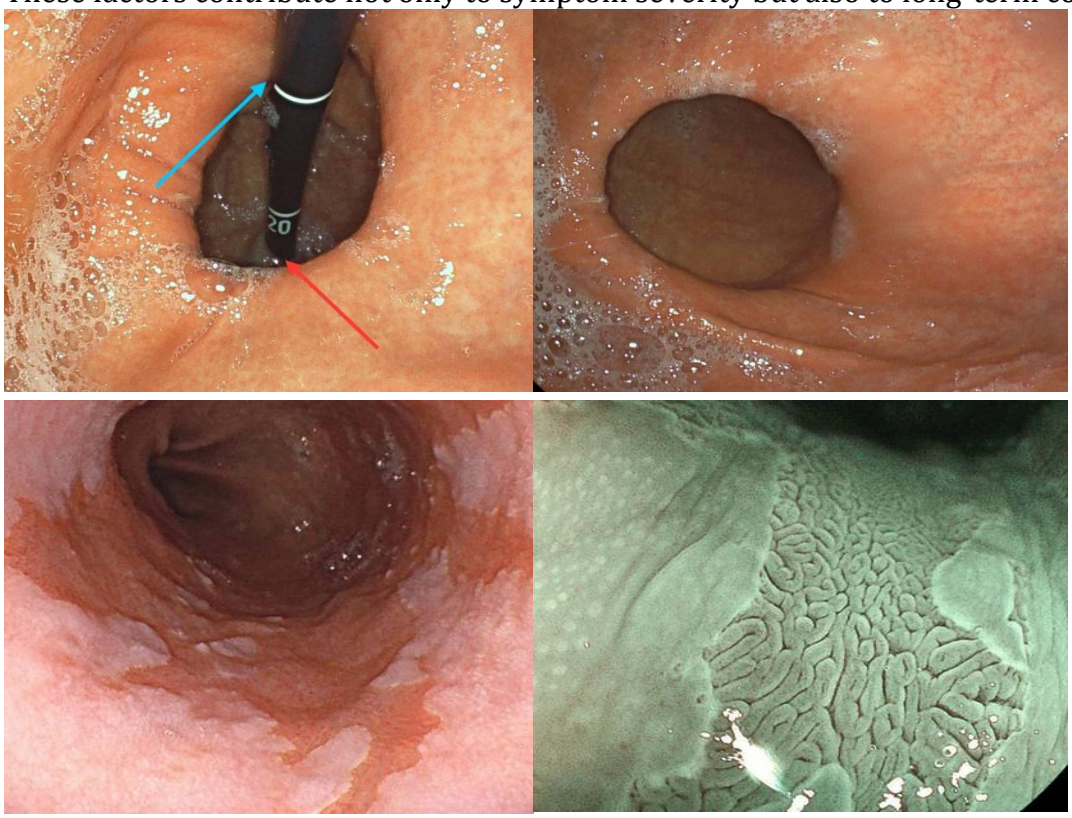

Figure 3. Endoscopic findings.
(A) Cardia insufficiency with incomplete closure of the lower esophageal sphincter.
(B) Barrett's esophagus with columnar epithelium and visible mucosal changes.

Discussion

The available evidence indicates that cardia insufficiency is not merely a functional abnormality but a key trigger of a complex, multistep pathological process.

Persistent reflux creates a microenvironment characterized by chronic inflammation and oxidative stress. These conditions favor epithelial remodeling and accumulation of genetic alterations, which are essential steps in carcinogenesis.

The transition from Barrett's esophagus to adenocarcinoma represents a classical example of inflammation-associated cancer development. However, this progression is influenced by multiple variables, including duration of exposure, individual susceptibility, and environmental factors.

From a clinical standpoint, early detection remains critical. Endoscopic surveillance with histological assessment is currently the most reliable method for identifying premalignant changes [1,2].

Pharmacological treatment, particularly with proton pump inhibitors, reduces acid exposure but does not fully eliminate cancer risk, highlighting the need for comprehensive management strategies.

Conclusion

Cardia insufficiency plays a fundamental role in the development of GERD and initiates a cascade of pathological changes that may lead to esophageal adenocarcinoma.

Chronic reflux promotes the formation of Barrett's esophagus and increases the likelihood of malignant transformation [8,13].

Clinical recommendations:

- regular endoscopic surveillance

- lifestyle modification (weight control, dietary changes)
- acid-suppressive therapy
- individualized risk assessment

A multidisciplinary approach is essential to improve outcomes and reduce cancer risk.

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