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MINI-REVIEW

Gastric Cancer: Introduction, Pathology, Epidemiology

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Gastric carcinoma is a malignant disease, which starts in the stomach. Despite declining incidence still remains the second cause of death of all malignancies worldwide. It is a major health problem for two reasons: In Asia, East Europe and developing countries the incidence decreases slowly. In USA and West Europe although incidence decreases sharply, mortality of diagnosed gastric cancer remains high.[1-4]

Adenocarcinoma of the stomach still remains a major health problem. There has been an decrease in incidence of this cancer worldwide but the degree of this reduction varies considerably among different geographical areas.

1. In USA and West Europe gastric cancer decreases dramatically in the last 50 years. In USA only 21,700 new gastric cancer cases are expected in 2001. However, despite advances in research and current treatment improvements, mortality of diagnosed gastric cancer remains very high.
2. In China (1,3 billion population), Japan, Korea and other East countries the decrease in incidence is much slowly and gastric cancer remains one of the most common malignancy and a leading cause of death from cancer.
3. In developing countries the decrease in incidence is also slow.[1-4]

The world's population is expected to increase from the current 6.1 billion to 9.3 billion during the next 50 years (United Nations Population Division) with Africa and Asia experiencing the greatest population growth. Since gastric cancer decreases there slowly, is expected an increased number of new cases in developing countries and Asia. The challenge of controlling the disease in these areas can not obviously resolved by endoscopic screening for early detection or sophisticated staging with subsequent tailored multidisciplinary approach which appear completely unrealistic now or in the near future. A rethinking about effective management strategy of the disease is needed.

The stomach is a sack-like organ between esophagus (a tube-shaped organ that carries food through the neck and chest to the stomach) and duodenum (first part of the small intestine). The stomach holds food and mixed it by secreting gastric juice into a thick fluid called chyme, which is then emptied into the duodenum. The stomach is divided into three different sections. The upper third, proximal stomach, closed to the esophagus is consisted of gastroesophageal junction (cardia) and fundus, the middle third of the stomach, the body and the lower portion (closed to the intestine) is the distal stomach consisted of the antrum and pylorus. Pylorus acts as a valve to control emptying of the stomach contents into the duodenum.

The stomach wall includes from the inner to out lining 4 layers, the mucosa, submucosa, muscularis propria, subserosa and serosa). The stomach has two curves, the lesser and greater curves, in which is attached the lesser and greater omentum respectively. Other organs next to the stomach, apart of esophagus and duodenum, are the colon, liver, spleen, and pancreas.

How does gastric carcinoma grow and spread?

Cells divided, grow and accumulated form tumors. Both benign and malignant tumors grow in an uncontrolled way. But it is only cells of malignant tumors that invade surrounding tissues, travel in blood and lymphatic systems and home into distant organs where they form secondary tumors (metastasis).[5-6]

Malignant primary gastric cancer cells at first confined into the mucosal layer (intra-mucosal cancers) and after a rather long natural history progress infiltrating the other layers of the wall stepwise (submucosa, muscularis propria, subserosa, serosa). When at diagnosis the cancer invasion is confined to mucosa or submucosal layer is defined as early gastric cancer (EGC), whereas invasion into muscularis propria or beyond it is defined as advanced gastric cancer

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(AGC). If stomach cancers left untreated, can spread and disseminate in a variety of forms: Through serosa infiltrating the adjacent organs (T4- cancers: spleen, transverse colon, liver, pancreas, etc). Due cancer cells which exfoliated from tumors penetrated serosal surface of the stomach (T3, T4- cancers).

These cells may implant and proliferate in peritoneal surface cavity leading to peritoneal carcinomatosis.

Due cancer cells that released from the original tumor and enter the lymphatic or blood circulation, migrate and form seconadary tumors (metastasis) in distant target-organs (liver, lung) and nodes.[5, 6]

The term gastric cancer or gastric carcinoma refers to adenocarcinoma of the stomach that accounts for around 90% of all stomach malignant tumors. The remainder malignant lesions of the stomach are gastric lymphomas (about 2%-7%) which in majority of cases are lymphoma of mucosa-associated lymphoid tissue (MALT-concept) and other rare tumors sush as gastric stromal tumors (sarcomas) developed from the muscle or connective tissue of the stomach wall, and carcinoid tumors.[7]

EPIDEMIOLOGY AND BIOLOGY

Incidence

The incidence of gastric adenocarcinoma decreases worldwide.[1-4,8,9] There have however been major geographical differences even among different areas in the same country. The incidence decreases dramatically in USA and many western European countries but much more slowly in far East (China, Japan, Korea), South America (Kolombia. Puerto Rico), Central Europe (Poland) and developing contries. In the USA, gastric cancer decreases now 1.4% per year and it is now only one-fourth (21700 new cases are expected in 2001 [1:www.cancer.org]) as common as it was in 1930.[1,3,9]

Why does gastric cancer incidence decrease?

The reasons for the decreased incidence of gastric cancer have not been elucidated. As possible factors have been reported a decreased consumption of salt-preserved foods and an increased consumption of fresh fruits and vegetables after the widespread introduction of refrigeration.[4-9]

Does declining incidence of gastric adenocarcinoma related to the sub-site (cardia/non-cardia)?

The declining incidence of gastric cancer in the USA and Western Europe largely reflects a decline in distal lesions, whereas, in contrast, there has been a steady rise in the incidence of adenocarcinoma of the proximal stomach and the gastroesophageal junction in the USA and Europe.[9-11] However, more recent data from Sweden indicate an overall decline in incidence of cancers distal to the gastric cardia by 9% [95% CI 6-12%] per year, but did not confirm a rise of cardia cancer which has been remained stable.[12]

Pathological Features

Gastric adenocarcinoma is classified according to WHO (adenocarcinoma, signet ring-cell carcinoma and undifferentiated carcinoma) but in the last years the Lauren-classification[13] into two major subtypes (intestinal type and diffuse type carcinomas) is now predominantly used worldwide.

Lauren classification

The histological classification of gastric carcinoma into the intestinal type and diffuse type is based on the criteria proposed by Lauren.[13] The proportion of intestinal type accounts for approximately 50%, that of the diffuse type 35% and the remainder 15% is characterized as "unclassified" or mixed type cancer.[13-16]

The intestinal type is characterized by cohesive neoplastic cells forming glandlike tubular structures, whereas in diffuse type cell cohesion is absent, so that individual cells infiltrate and thicken the stomach wall without forming a discrete mass. This difference in microscopic growth pattern is also reflected in the different macroscopic appearance of the two histological subtypes.[13] Whereas for intestinal type the macroscopic margins correspond approximately to the microscopic spread, the diffuse type as a poorly differentiated cancer can extend submucosally far beyond its macroscopic borders. This difference in tumor spread of the two types of Lauren-classification is of clinical importance in decision-making about appropriate treatment option.

The intestinal type predominate in high-risk areas, occur more often in distal stomach, and is often preceded by a prolonged precancerous phase, whereas diffuse tumors prevail among young patients and women and the contribution of hereditary factors to their causation is higher.[9]

WORLD Health Organization (WHO) - and Lauren classification: How to combine?

In several reports now the WHO-classification is used while in some others the histologic classification according to the Lauren. Thus, there is confusion among phycisians. It is therefore useful and of practical value to see whether these two classifications systems can easily and simply be combined. Indeed, in general, well and moderately differentiated cancer of WHO correspond to intestinal type according to Lauren, whereas poor differentiated or undifferentiated or signet ring cell - carcinoma to the diffuse type carcinoma respectively.[4]

Is there a difference in time trends incidence of the two histologic subtypes?

The decline in overall incidence of gastric carcinoma during this century appears to be largely attributable to a decrease of the intestinal type lesions, while the occurrence of diffuse type is thought to have remained more stable.[9,14,15] Most recent epidemiological data from North Europe (Sweden) however, indicate that both types decline markedly, at similar rapidity, and

with no significant trend differences between the intestinal and diffuse types.[17]

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