Re-Evaluation of Resection margin in Gastrointestinal Tract Neoplasms Based on DNA Pattern and Histopathology

Thesis

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By

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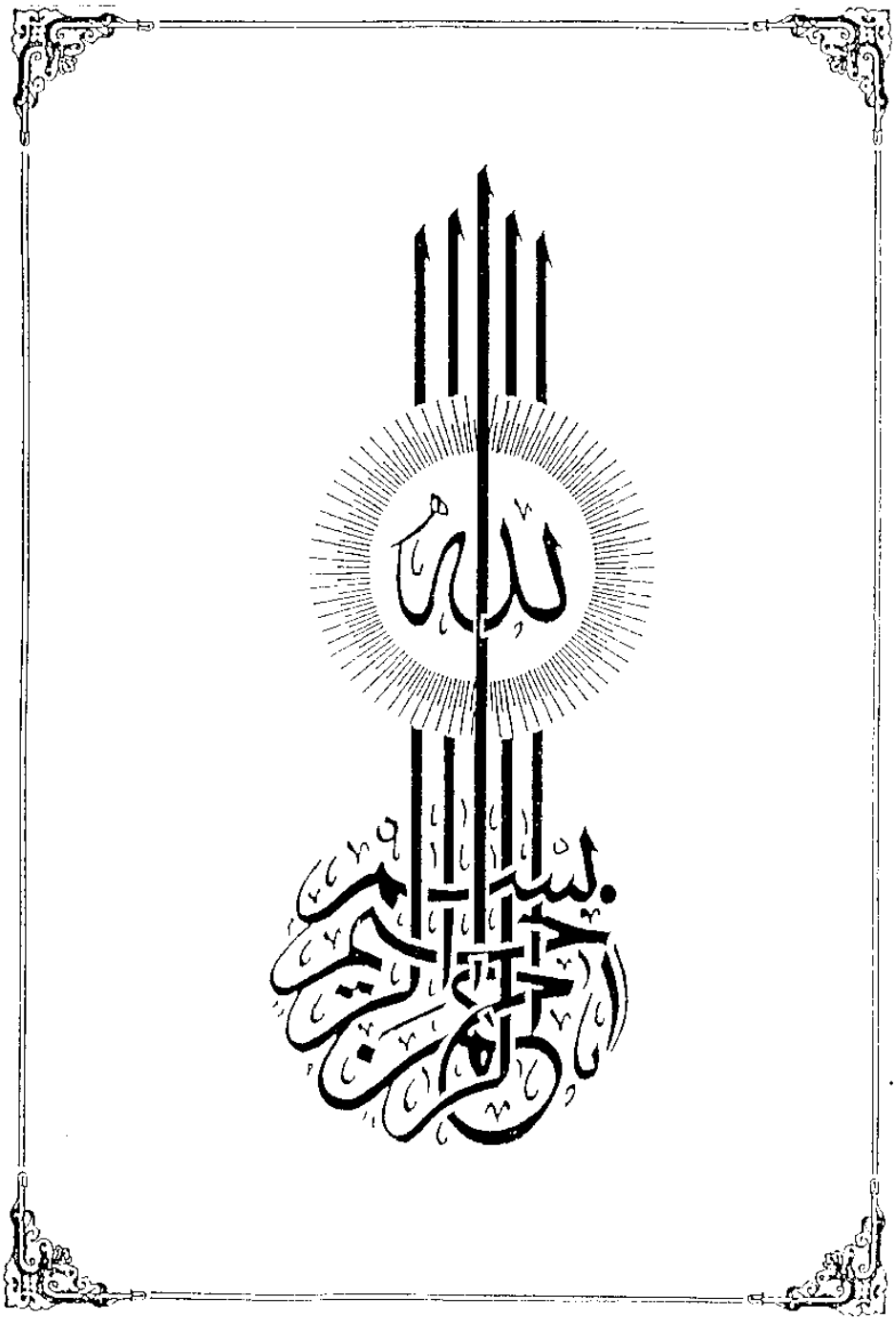

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Gastrointestinal tract tumors are a common malignancy and a major cause of cancer morbidity and mortality worldwide. To understand the mechanisms of GIT carcinogenesis, abnormalities in DNA content of GIT tumors were studied. A statistically significant relationship was found between the degree of differentiation of the tumor and DNA content abnormalities. (Robaszkiewicz . et al, 1991).

Recent studies on dysplasia have shown the following two problems, the classification of dysplasia which is subjected to inter and intra-observer variation as well as the interpretation which is particularly difficult when there is acute inflammation (Filipe et al 1985; Collins et al 1987; Fozard et al 1989).

Solving these problems has prompted a research for more objective methods of determing dysplasia such as the analysis of DNA contents (Riddle et al 1985). DNA content (ploidy) measured by DNA flow cytometry was shown to correlate with several clinicopathological characteristics in several types of tumors (Kyoo et al 1993).

DNA flow cytometry is a powerful technique that can measure DNA content (ploidy) and proliferative activity (S-phase fraction) of tissues rapidly and quantitatively (Dressler et al 1989), in several types of tumors, DNA Ploidy and s-phase fraction were shown to be significant independent diagnostic and prognostic parameters. (Kimura et al 1991).

The aneuploid cell populations can be defined as those that contain an abnormal number of chromosomes or an abnormal amount of DNA. Aneuploidy can be reliably detected by flow cytometric analysis of DNA content. This technique not only identifies aneuploid cell populations but can also quantify the percent of cells in various phases of the cell cycle, thus giving an indication of the proliferative activity of a tissue. Transitional mucosa adjacent to carcinomas of different parts of GIT shows histologic and mucin histochemical changes that may indicate premalignant changes and may be of prognostic value (Ahnen DJ 1992; Wang et al 1992).

The present work aims to evaluate the resection limits of the different parts of gastrointestinal tract in malignancy based on DNA pattern measured by flow cytometry as a helpful and more accurate method in detecting the extent of local precancerous changes beyond the gross edges of the main neoplasm. The findings may help in choosing the proper procedure for local surgical management and limits of resection.

Surgical Anatomy

Surgical Anatomy
Of Gastrointestinal tract

Gastrointestinal tract is a long muscular hollow tube, which is modified to achieve various functions as digestion, absorption, excretion, together with secretion of digestive hormones. It constitutes various regions from above downward, stomach, small and large intestine, rectum and anal canal.

Surgical Anatomy of the Stomach

The stomach is an expanded part of the GIT responsible for the initial breakdown and predigestion of a meal. Due to its reservoir function, the stomach has a variable shape depending on the volume of fluid or food it contains. The position of the stomach varies, according to whether the person is in the erect or supine position. It is located in the upper abdomen beneath the left hypochondrium and this allows for free expansion of its wall. The stomach is divided into fundus, body, and pylorus (antrum).

The fundus receives and stores solid foods that pass into it from the esophagus above. The thicker walled more muscular distal portion of the stomach, *the antrum*, grinds and mixes the food and then forces it back into the fundus for further reduction in size and predigestion. Small particles move forward into the duodenum where they are further processed by intestinal secretions. A thick band of circular smooth muscle, *the pyloric sphincter*, delineates the distal stomach. This sphincter prevents duodeno-gastric reflux and regulates gastric emptying by relaxing during anteral propulsive contraction. (Griffith, 1969).

The fundus of the stomach is lined by a highly specialized epithelium that secretes hydrochloric acid, pepsin and intrinsic factor. The mucosa of the antrum participates in the process of gastric acid secretion by releasing the secretagogue (gastrin) into the circulation. This event is mediated by vagal release of acetylcholine and is modulated by the PH of the antral lumen. The stomach therefore can be considered as two organs, its proximal portion is designed for storage and digestion while its distal portion is adapted to the role of mixing and evacuation. (Lillibridge 1964).

The relationships of the stomach to other intra-abdominal organs (fig.1) are very important in many diseases. The most important adjacent organs are the pancreas and liver which lie dorsal and ventral respectively and the spleen which lie directly to the left of the greater curvature of the stomach. Inflammation of the pancreas may delay gastric emptying, while enlargement by neoplasm may cause a sense of fullness or even obstruction to the gastric outlet. Liver or splenic enlargement may also interfere with the storage capacity of the stomach by encroachment on its lumen, the transverse colon which lies caudally may also interfere with gastric function by direct neoplastic extension (Cook 1975).

More commonly the stomach affects adjacent organs by direct extension or penetration from a gastric carcinoma. Another closely related structure is the biliary tree. It runs posterior to the first part of the duodenum only a few centimeters from the gastric outlet and is vulnerable to injury not only from gastric tumors but also from attempts at treatment by gastrectomy (Cook 1975).

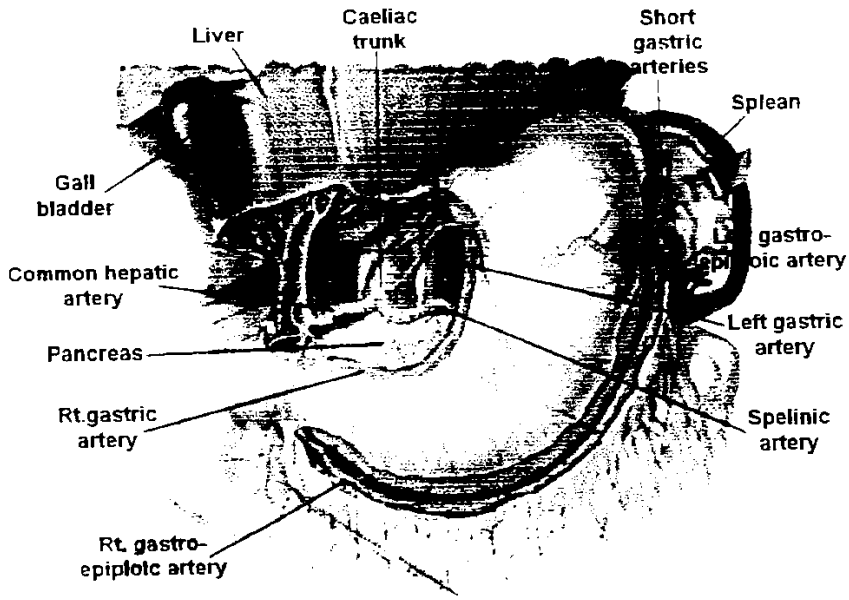

Fig. (1) Blood supply and relations of the stomach

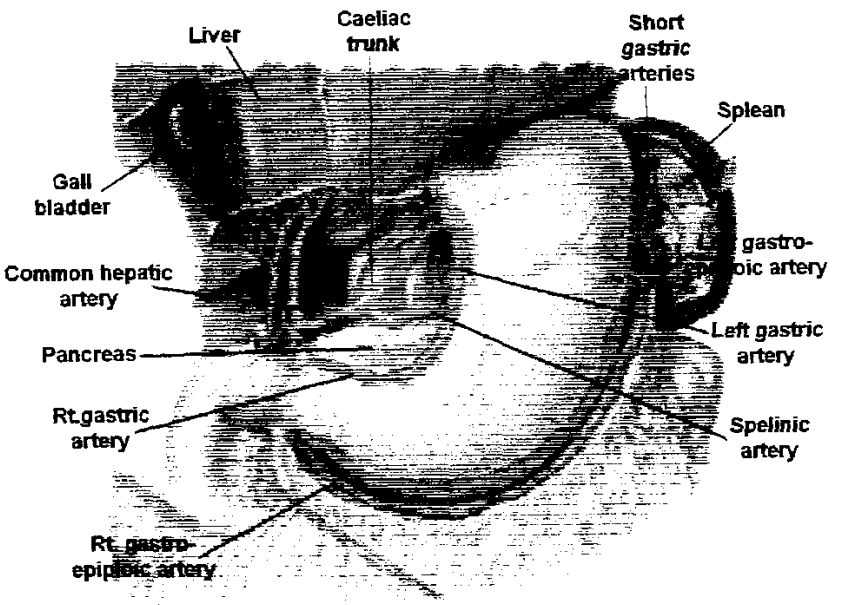

Fig. (1) Blood supply and relations of the stomach

Blood Supply of the Stomach (fig. 1)

The stomach has a blood supply so extensive and interconnected that three of its four major nutrient arteries can be ligated without causing necrosis or even significant dysfunction. A submucosal plexus of arterioles provides for rapid healing of wounds and a low incidence of anastomotic disruption after operative manipulation. Because of this vascularity, mucosal lesions may bleed extensively even when small or superficial. As regard ***arterial supply of the stomach***, there are four main arteries. *The left gastric artery* arises from the coeliac axis and divides into an ascending (esophageal) branch and a descending branch. The descending branch, lying between the layers of the lesser omentum, is closely opposed to the lesser curvature and sends branches to the stomach. *The right gastric artery* arising from the common hepatic artery. It is divided into a number of branches to the stomach along the lesser curvature and anastomose with the left gastric artery. *The right gastro-epiploic artery* arises from the gastro-duodenal artery, and anastomose with the left gastro-epiploic vessel with which it forms an arcade supplying the greater curvature. The gastro-duodenal artery itself arises from the hepatic artery, and pass down behind the duodenum. It is often the artery that is eroded and is the source of bleeding in duodenal ulceration. *The left gastro-epiploic artery*, arises from the splenic artery and contributes to the arterial arcade along the greater curvature. Five to seven small branches arise from the splenic artery to supply the fundus called *short gastric arteries*.

The anstomosis between the two main epiploic arteries takes place 2 to 3 cm. from the greater curvature to form the gastro-epiploic arch, which send branches to supply the greater omentum. In such cases this epiploic

arcade may be ligated during mobilization of the omentum and this may result in necrosis of part of the greater omentum if the right or left epiploic artery is also ligated (Bentley and Borlow; 1952)

The vessels to the mucosa of the lesser curvature do not arise from a submucous plexus in the stomach wall, as do the vessels elsewhere in the gastrointestinal tract, but directly from the left or right gastric arteries outside the gastric wall. These small mucosal vessels must then run a long course, piercing the serosa, muscle and the lamina muscularis mucosa, to reach the mucosa. The long course of these vessels and the lack of submucosal plexus are thought to be factors that are responsible for the development of lesser curvature ischaemia and perhaps ulceration. (Lawson, 1986)

The veins of the stomach mainly accompany the arteries. Of particular surgical importance is the left gastric vein, which receives branches from the esophagus. This vein must be divided especially in operation for bleeding esophageal varices. (Bently and Barlow; 1952)

Lymphatic drainage of the stomach (fig. 2) follows the distribution of the blood supply. An understanding of lymphatic channels and their nodal communication is important to assessment of tumor spread from gastric carcinoma. Divide the stomach by a line in its long axis, two-thirds of the stomach being to the right of this line, one-third to the left. Divide the left third into two by a line at the junction of its upper third and lower two-thirds. This marks out the three lymph regions of the stomach. So lymphatics from the lesser curvature of the stomach drains into left gastric and suprapancreatic nodes (superior group). Lesions high on the greater

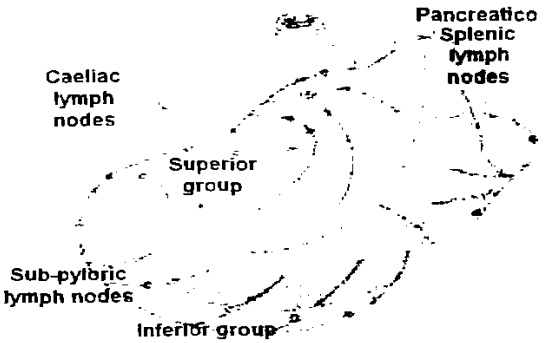

Fig (2.a) Lymph drainage of the stomach

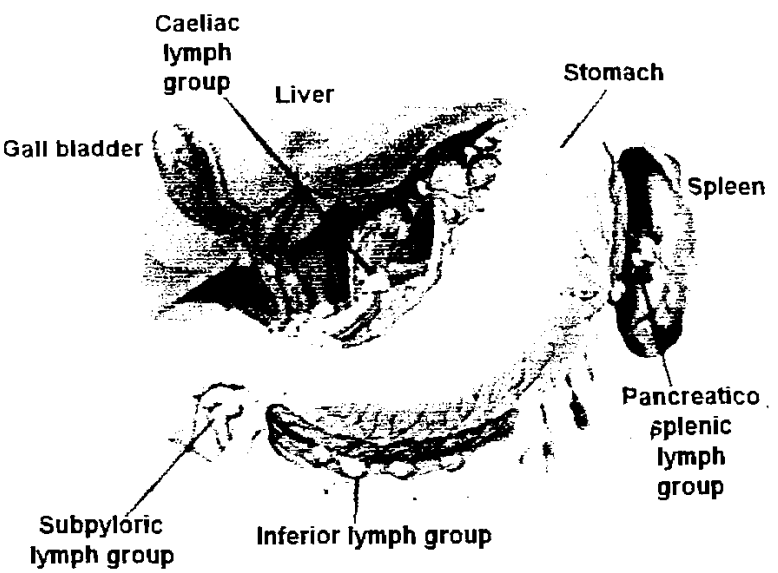

Fig (2.b) Lymph nodes of the stomach