Chapter 9

Early Gastric Cancer: Surgery or Endoscopy?

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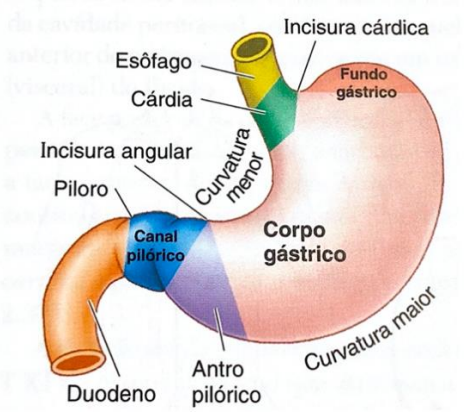
ABSTRACT

Gastric cancer is an extremely important issue, responsible for the fifth leading cause of cancer death in Brazil. It has a higher incidence in men than women, but usually over 60 years of age. There is no doubt that its early detection guarantees a longer survival and, as in the literature there is still a question about the therapeutic approach of early gastric cancer, we decided to study it. The objective of this work was to perform a horizontal review of the PRISMA method to evaluate the best treatment for cases of early gastric cancer: surgery or endoscopy. Six independent reviewers placed the keywords "comparison", "submucosal endoscopic dissection", "surgical resection", "early gastric cancer", "early gastric cancer", "treatment", "surgery" and "endoscopic" in the PubMed database and obtained seventy-one articles. The inclusion criteria were adults with early gastric cancer and who underwent surgical or endoscopic laparoscopic therapy and exclusion ary patients were articles in a language other than English; Duplicate; articles that did not address the comparison between techniques of resection of early gastric cancer; articles published before 2015. Given the controversy among surgical or endoscopic therapies of early gastric cancer, the aim of this study was to analyze the revised and indexed literature in order to choose which therapy is best. After a detailed analysis of each article, nineteen of them were elected and the outcomes were as follows: in relation to the overall survival rate, among the results of the past there was a prevalence of better survival outcomes on gastrectomy, but the non-difference in the results obtained is probably due to advances in endoscopic techniques that provide lower rates of error in the procedure and greater precision in tumor removal. Regarding the adverse event rate, there was a prevalence in the results of lower rates of adverse effect on endoscopic resection (ESD) and this is probably due to the higher risk of infection that open surgery brings. Moreover, the endoscopic technique is less invasive and maintains the anatomical integrity of the stomach. Regarding the risk rate, although the result is inconclusive, it is much discussed that the risk of perforation is higher in endoscopy because it is a procedure with a lower field of surgical view. However, with advances in endoscopic technique, this risk tends to decrease as time goes by. Regarding the recurrence rate, fourteen articles obtained concrete data to conclude that recurrence rates were significantly higher in the group that underwent endoscopic resection when compared to the group submitted to gastrectomy. This is probably justified by the non-total resection of the tumor by endoscopic technique compared to gastrectomy, due to the lower visual field during the procedures and lower mobility of the surgeon. Regarding the time of hospitalization, all concluded that patients undergoing endoscopic resection had shorter hospital stay. A hypothesis for this fact would be the smaller incision in the patient and because it is a smaller surgery, having fewer adverse events with lower risk of infection, which provides a faster recovery. Finally, in relation to cost, all concluded that endoscopic resection is less costly than surgery. This is due to the fact that, because it is a smaller surgery, it requires fewer materials, anesthesia, auxiliary professionals, requires a shorter hospitalization time and has fewer adverse effects. That said, endoscopic resection proved to be more efficient in the treatment of early gastric cancer, except for the recurrence rate.

1 INTRODUCTION

1.1 ANATOMY

The stomach is divided into 4 parts: cardia (part surrounding the cardial ostium, transitions from the esophagogastric junction and bottom and is at the level of the thoracic vertebra T11); bottom (consists of the upper and dilated part of the organ; through the cardial notch binds to the proximal esophagus; can be dilated by gas, liquid or food; is located after the 7th left rib and is related to the hemidiaphragm left and spleen); body (it is the part between the gastric fundus and the pyloric den, it is the majority of the stomach and is characterized by the presence of "wrinkles"); pyloric part (divided into 4 parts: pyloric den, wider part leading to the pyloric canal (narrower). The pyloric is the distal sphincter region of the pyloric part that controls the output of gastric contents to the duodenum through the pyloric ostium, which is the lower opening of the stomach. In addition, the stomach has two curvatures: the greater curvature, which corresponds to the convex and longer margin of the organ, located lower; and the smaller curvature corresponding to the most concave and smaller margin of the organ, has the angular notch as lower delimitation, which indicates the junction of the gastric body to the pyloric part. [1st]



The stomach has the function of storing food and performing part of the enzymatic digestion. Gastric juice, a product of gastric secretion, transforms the food into "chemo", a mixture that will be transported to the duodenum. At the bottom and in the body of the stomach is the acid-producing region, in which there is the presence of gastric glands that contain parietal cells that secrete intrinsic factors and the acid itself. In addition, these glands also have zimogen-rich cells that produce pepsinogen, which when in contact with hydrochloric acid is activated in its form of pepsin that performs the digestion of proteins. The gastric mucosa of the stomach body, as well as a part of the bottom and pyloric den have parietal cells, which have as their function the production of hydrochloric acid that activates pepsin in pepsinogen and decreases bacterial colonization in the stomach and duodenum due to its low pH. [2nd]

Gastric secretion can be divided into 3 phases: cephalic, gastric and intestinal. In the cephalic phase, the secretion of hydrochloric acid is mediated by vagal excitation that occurs before a feeling of smell, thought, vision and even the taste of food. Vagal excitation causes increased acetylcholine, which stimulates the secretion of acid and pepsin by the parietal and main cells, respectively. The gastric phase is mediated by gastric distension, that is, as soon as the food enters the stomach mechanical distension occurs, and it is at this stage that most of the secretion occurs besides having gastrin release by g cells. This causes increased secretion of the secretin hormone, which promotes decreased intestinal motility, preventing more food from going into the duodenum. In addition, it also acts on the stomach glands and inhibits the secretion of hydrochloric acid. [3rd]

Previously the stomach relates to the diaphragm, the left hepatic lobe and the anterior wall of the abdomen; already later relates to the pancreas. Moreover, there is less relationship with the transverse neck of the large intestine. [1st]

The stomach is irrigated by arteries derived from the celiac trunk and its branches, such as the right and left gastric arteries and the short and posterior gastromental arteries that irrigate mainly the minor and greater curvature, respectively. Venous drainage is performed by the right and left gastric veins that drain into the portal vein, the left gastromental veins and short gastric veins drain into the splenic vein and the right gastromental vein that drain into the superior mesenteric vein. [4th]

The stomach is located between the proximal esophagus and the distal duodenum. The lower esophageal sphincter creates a high pressure zone under normal conditions that prevents gastric contents from returning to the esophagus. Similarly, the pyloric sphincter performs this same function, preventing reflux of the duodenal content to the stomach. [5th]

2 GASTRIC DISEASES

The stomach is an organ that can be affected by various diseases, such as: diseases from neuromuscular disorders; gastric secretion disorders; gastritis; peptic ulcerative disease.

2.1 GASTRIC NEUROMUSCULAR DISORDERS

Gastric neuromuscular disorders include contractile and electrical dysfunctions. At one end of this spectrum are gastric arrhythmias, which are sudden electrical disturbances associated with severe symptoms of nausea. Abnormalities in relaxation of the gastric fundus are associated with early satiety. At the other end of this spectrum, anthral hypomotility and deep gastroparesis are associated with prolonged postprandial satiety, vomiting, swelling, weight loss, and malnutrition, which may make enteral or parenteral nutritional support necessary.

Disorders of gastric secretion:

Patients with duodenal ulcer manifest increased acid gastric secretion. It is known that most cases of duodenal ulcer are due to H. pylori infection, and that this infection is responsible for gastric secretion disorders in these patients. In contrast, patients with gastric ulcers have normal or decreased acid production, although often these patients also have H infection. Pylori. This suggests that a change in the defense of the gastric mucosa may have a crucial pathophysiological importance. [6th]

Gastritis:

The term 'gastritis' is used under different definitions. Some authors argue that gastritis is a complex symptom. Others argue that this is a description of an endoscopic finding of the stomach. Other authors use the term to describe a microscopic inflammation of the stomach. Sleisenger and Fordtran use this third definition in their book Gastrointestinal tract and liver diseases. There is no clear relationship between the presence of microscopic inflammation and gastric symptoms (epigastralgia, nausea, vomiting, bleeding).

The correlation between microscopic and endoscopic abnormalities is also poor. Most patients with histological gastritis are asymptomatic and have normal endoscopic findings. [7th]

2.2 PEPTIC ULCERATIVE DISEASE

2.2.1 Peptic ulcer

A gastrointestinal tract ulcer can be defined as a rupture in the mucosal lining, with considerable depth in endoscopy, or histological evidence of submucosal involvement. Earthlings are ruptures on the surface of the epithelium that do not have noticeable depth. The term 'peptic ulcer disease' is widely used to include ulcerations and erosons in the stomach and duodenum, from various causes. This is because pepsin, which is proteolytic in acid solution, plays a large role in mucosal rupture, regardless of the causative agent of such a condition (e.g.: H. pylori, aspirin or an IANES.).

The main risk factors for peptic ulcer are H. pylori infection and use of NSAID. However, some patients with peptic ulcer disease do not have any of these risk factors.

Classic symptoms of peptic ulcer disease include burning pain in epigastrium, relieved by antacids. These aspects were challenged with the advent of endoscopy, which made it clear that the same symptoms were also present in patients without visible abnormalities on endoscopy.

The gold standard test for diagnosis of peptic ulcer disease is endoscopy. Its main limitation is its high cost in certain countries, such as the U.S. The decision to perform the EDA is based on different factors. Patients who have complications of peptic ulcer disease such as bleeding require endoscopic evaluation in case of an accurate diagnosis. The presence of alarm factors, such as weight loss or recurrent vomiting, may be evidence of malignancy. Although AED is considered the gold standard test for the diagnosis of peptic ulcer disease, small ulcers may not be visible on examination. Among the complications of peptic ulcer disease, hemorrhage, penetration, perforation and obstruction should be emphasized. [8th]

3 GASTRIC NEOPLASIA

Definition:

Neoplasia literally means "new growth". Neoplastic cells are said to be transformed because they continue to replicate, apparently "inattentive" to the regulatory influences that control normal cell growth. Neoplasms, therefore, enjoy a certain degree of autonomy and tend to increase in size regardless of their local environment. Its autonomy, however, is not absolutely complete. Some neoplasms require endocrine support, and such dependencies can sometimes be explored therapeutically. All neoplasms depend on the host for their nutrition and blood supply. In common medical use, usually a neoplasm is referred to as tumor, and the study of tumors is called oncology (of oncos, "tumor", and logos, "study of"). Among tumors, the division of neoplasms into benign and malignant categories is based on the judgment of the potential clinical behavior of a tumor.

It is said that a tumor is benign when its micro and macroscopic features are considered relatively innocent, indicating that it will remain localized, and is treatable with surgical removal; usually the patient survives. It should be noted, however, that benign tumors can produce more than localized masses and are sometimes responsible for severe disease.

Malignant tumors are collectively referred to as cancers, a term derived from the Latin word "crab" — that is, they cling to any part where they cling and obstinately, similar to the crab's behavior. The term malignant applies to a neoplasm indicating that the lesion can invade and destroy adjacent structures and spread to distant sites (metastases) to cause death. Not all cancers continue on such a deadly course. The more aggressive are also some of the most curable, but the evil designation constitutes a red flag.

All tumors, benign and malignant, have two basic components: (1) the parenchyma, consisting of neoplastic or transformed cells, and (2) the stroma, consisting of connective tissue, blood vessels and inflammatory cells derived from the host. The parenchyma of the neoplasm mainly determines its biological behavior, and it is from this component that derives its name. Stroma is crucial for the growth of neoplasia, since it contains the blood supply and supports the growth of parenchyma cells. Although the biological behavior of tumors mainly reflects the behavior of parenchyma cells, there is a growing perception that stromal and neoplastic cells maintain a two-way "conversation" that influences tumor growth.

3.1 BENIGN GASTRIC NEOPLASIA:

3.1.1 Gastric Polyps

Polyps, nodules or masses that protrude above the level of the surrounding mucosa are identified in up to 5% of upper gastrointestinal tract endoscopies. Polyps may develop as a result of epithelial and stromal cell hyperplasia, inflammation, ectopy, or neoplasia. Although many different types of polyps may occur in the stomach, only hyperplastic and inflammatory polyps, polyps of fungal glands and adenomas are considered here.

3.1.2 Inflammatory and Hyperplastic Polyps

Approximately 75% of all gastric polyps are inflammatory or hyperplastic polyps. Most commonly, they affect people between 50-60 years of age, usually from a fundof chronic gastritis that initiates the lesion and the reactive hyperplasia that causes polyp growth. If associated with gastritis by H. pylori, polyps may regress after eradication of the bacterium.

3.1.3 Polyps of Fungal Glands

Polyps of fungal glands occur sporadically and in people with family adenomatous polyposis (PAF), but have no neoplastic potential. However, it is worth mentioning them here because their incidence has increased sharply as a result of the use of proton pump inhibitors. This probably results from increased gastrin secretion in response to reduced acidity and gastrin-driven glandular hyperplasia. Polyps of the

fungal glands may be asymptomatic or associated with nausea, vomiting, or epigastric pain. These well-circumscribed polyps occur in the gastric body and fundus, often multiple and composed of irregular glands, cystically dilated , coated with flat and main parietal cells.

3.1.4 Gastric Adenoma

Gastric adenomas account for up to 10% of all gastric polyps. Its incidence increases with age and varies between different populations in parallel with gastric adenocarcinoma. Patients are usually between 50-60 years of age, and men are three times more often affected than women. Similar to other forms of gastric dysplasia, adenomas almost always occur when a history of chronic gastritis with intestinal atrophy and metaplasia. The risk for the development of adenocarcinoma in gastric adenomas is related to the size of the lesion and is particularly high with lesions larger than 2 cm in diameter. In general, carcinoma may be present in up to 30% of gastric adenomas. [9th]

3.1.5 Malignant Gastric Neoplasia:

Gastric tumors are defined in benign or malignant, according to their metastasis potential. Gastric adenocarcinoma make up most malignant tumors. Other types of malignant gastric cancer are: lymphoma, carcinoid tumor, stromal gastrointestinal tumor, various tumors.

Gastric lymphoma accounts for approximately 3% of malignant gastric tumors, and can be subdivided into primary and secondary (nodal spread to the stomach). More than 95% of gastric lymphomas are non-Hodgkin's type, the most common form of extranodal non-Hodgkin lymphoma, with more than 30% of cases. In endoscopy, it can manifest in several forms such as: fungal lesions, polypoid masses, thickened gastric folds, or ulcerative lesions.

Carcinoid gastric tumor corresponds to 7% of all gastrointestinal carcinoid tumors and 0.2% of gastric neoplasia. Gastrointestinal stromal tumors (GIST) are nonepithelial intra-abdominal (mesenchymal) and may develop throughout the gastrointestinal tract. Of all GIST occurring in the gastrointestinal tract, 50% to 60% occur in the stomach. Metastatic disease in the stomach can occur with melanoma or primary cancers in the breast, lung, ovary, liver, colon and testicles. [10th]

3.1.6 Types/Classification:

There are different classifications for gastric neoplasia. One of the classifications were described by Borrmann based on gross appearance: polypoid, fungal, ulcerated and infiltrative. This classification is old but still useful, as this macroscopic growth has relevance for microscopic classification. Another classification is that of Lauren, which was described in the 1960s, which is based according to the pattern of glandular growth, which can be intestinal or diffuse. However, there is a problem with Laurén classification because 15 to 20% of carcinomas cannot be classified in any of the groups. Finally, Ming classified gastric carcinomas into two types, those with expanding growth pattern and those with infiltrative

growth pattern. The World Health Organization (WHO) classification system distinguishes between the subtypes of papillar, tubular, mucinous and synet ring cells. This classification is used by many and can be useful. However, Lauren's classification remains one of the most widely used. [11th]

There are also subtypes of the disease that are divided into: non-cardic, diffuse and proximal. This classification into subtypes is the most recent. And there are studies that correlate this subtype with risk factors and epidemiology. [12th]

Summary of Environmental, Clinical, and Genetic Risk Factors Associated with Gastric Cancer			
Gastric Cancer Subtype	**Epidemiology/Biology**	**Prevalent Risk Factors (Estimated OR)**	
Non-cardia gastric cancer	**Significant geographic variation, more common in high-risk areas**	**Environmental**	**High dietary salt Eating fruits/vegetables (OR, -0.7) Tobacco (OR, -1.5)**
	Chronic inflammation leads to stepwise progression: metaplasia, dysplasia, atrophic gastritis, malignancy	**Clinical**	**Age (peak at 50-70 y) *H pylori* infection (OR, - 3.0) Use of NSAIDs/aspirin**
		Genetic	**Family history (OR, 2.0-6.0) Imunne regulatory SNPs HNPCC**
Difuse gastric cancer	**Uniform distribution worldwide**	**Environmental**	**None specifically identified**
	Incidence rising	**Clinical**	***Helicobacter pylori* identified**
	Established genetic predisposition syndrome	**Genetic**	**CDH1 mutation Family history (non-CDH1 mutant)**
	Often grouped with gastroesophageal junction and distal esophageal adenocarcinoma	**Environmental**	**Tobacco use Alcohol use**

Gastric proximal cancer	**Incidence rising significantly in industrialized nations**	**Clinical**	**Obesity/High BMI GERD**
		Genetic	**None specifically identified**
Abbreviations: BMI, body mass index; GERD, gastroesophageal reflux disease; HNPCC, hereditary nonpolyposis colorectal cancer; NSAID, nonsteroidal anti-inflammatory drug; OR, odds ratio; SNP's, single nucleotide polymorphism			

3.1.7 Staging

The staging system used for stomach cancer is the TNM system of the American Joint Committee on Cancer. The TNM system uses three criteria to evaluate the stage of cancer: the tumor itself, the regional lymph nodes around the tumor, and whether the tumor has spread to other parts of the body. TNM is short for tumor (T), lymph node (N) and metastasis (M): **T.** Indicates the size of the primary tumor and has spread to other areas. **N. Describes** whether there is dissemination of the disease to regional lymph nodes or if there is evidence of metastases in transit. **M. Indicates** whether there is metastasis in other parts of the body.

Tumor. By the TNM system, T accompanied by a number (0 to 4) is used to describe the primary tumor, particularly its size. A lowercase letter "a" or "b" can also be assigned based on ulceration and the istic rate.

Lymph node. The N in the TNM system represents the regional lymph nodes, and it is also assigned a number (0 to 3), which indicates whether the disease has spread to the lymph nodes. A lowercase letter "a", "b", or "c" can also be assigned as described below.

Metastasis. The M in the TNM system indicates whether the disease has spread to other parts of the body.

3.1.8 Primary Tumor (T)

TX. The main tumor cannot be evaluated.

T0. No sign of tumor was detected.

Tis. Cancer cells are only in the upper layer of the mucosa and have not invaded the deepest layers of tissue. This stage is called in situ.

T1. The tumor developed from the upper mucosa to the lower layers, near the submucosa.

T1a. The tumor is developing in the muscular part of the mucosa.

T1b. The tumor developed in the muscular part of the mucosa and in the submucosa.

T2. The tumor is developing into the muscle layer.

T3. The tumor is developing into the subserous layer.

T4. The tumor developed in the stomach wall and serosa, and may have already reached another organ (such as spleen, intestines, pancreas, kidney) or other structures such as blood vessels.

T4a. The tumor developed from the stomach wall to the serosa (outer lining of the stomach), but did not reach adjacent organs and structures.

T4b. The tumor developed in the stomach wall and has already reached neighboring organs and structures.

3.1.9 Regional Lymph nodes (N)

Nx. Regional lymph nodes cannot be evaluated.

No, no, no, no The lymph nodes are free.

No. The cancer spread to 1 or 2 lymph nodes nearby.

N2. The cancer spread to 3 to 6 lymph nodes.

N3. The cancer has spread to 7 or more lymph nodes.

N3a. The cancer spread to 7 to 15 lymph nodes.

N3b. Cancer has spread to more than 16 lymph nodes.

3.1.10 Distant Metastasis (M)

M0. Absence of distant metastases.

M1. Distant metastases.

3.1.11 Stages of Cancer

Stage 0. Tis, N0, M0.

Stage IA. T1, N0, M0.

Stage IB. T1, N1, M0; T2, N0, M0.

Stage IIA. T1, N2, M0; T2, N1, M0; T3, N0, M0.

Stage IIB. T1, N3, M0; T2, N2, M0; T3, N1, M0; T4a, N0, M0.

Stage IIIA. T2, N3, M0; T3, N2, M0; T4a, N1, M0.

Stage IIIB. T3, N3, M0; T4a, N2, M0; T4b, N0 or N1, M0.

Stage IIIC. T4a, N3, M0; T4b, N2 or N3, M0.

Stage IV. Any T, any N, M1. [13th]

4 PATHOPHYSIOLOGY

4.1 H. PYLORI.:

Helicobacter pylori infection, a carcinogenic bacterium, is the biggest risk factor for gastric cancer - a disease that kills hundreds of thousands of lives a year. Approximately 75% of the overall burden of gastric cancer and 5.5% of malignant diseases worldwide are attributable to H-induced inflammation and injury. pylori, but the precise mechanisms that regulate the development of cancer in response to this organism are much less defined.

In many regions of the world, rates of H. pylori infection and gastric cancer are concordant; in Asia, high prevalence rates of H pylori reflect the high prevalence of gastric cancer. However, this association is not universal. For example, the prevalence of H infection. pylori in Africa is high, but the frequency of gastric cancer is extremely low. In Colombia, the prevalence of H pylori is also very high throughout the country (> 90% of individuals are infected), but individuals residing in the mountains have high rates of gastric cancer (150 cases / 100,000), while those on the coast have very low rates (6 cases / 100,000). This disparity in the prevalence of gastric cancer, but not H. provided a unique opportunity to evaluate the effects of h interactions. pylori and human ancestry in gastric carcinogenesis.

Gastric atrophy has a lower risk of progression to cancer than metaplasia or intestinal dysplasia. A recent study from Sweden predicted that 1/256 people with normal mucosa, 1/85 people with non-atrophic gastritis, 1/50 people with atrophic gastritis, 1/39 people with intestinal metaplasia and 1/19 people with dysplasia developed gastric cancer in 20 years. Similarly, people at the lowest levels (5th percentile) of Amerindian ancestry, but with high African ancestry infected with H pylori strains with high African genetic content, are expected to have only gastritis. The interactions between the host and pathogen ancestors, therefore, have completely explained the differences in the severity of gastric injury in these populations; only human genetic or H pylori variation is not sufficient to determine susceptibility to the disease - a genetic incompatibility is also required. This discovery implies that the constant genetic adaptation of individual H pylori strains to their particular hosts reached a balance that was interrupted by the acquisition of incompatible strains when several human populations began to blend. An important next step for co-evolutionary studies is to identify differential patterns of concerted selection in paired human and pathogenic loci obtained from other global populations, such as Asia, which differ in terms of cancer risk, human ancestry, and genetic variation of H. Pylori.

The risk of developing gastric cancer depends on a set of interacting components, including virulence factors specific to the H pylori strain, host genotype, environmental factors such as diet, as well as alternation in stem cell populations and the microbiome. Molecular interactions between these factors affect the result of long-term colonization of H. pylori. [14th]

4.2 ENVIRONMENTAL FACTORS:

A 2018 systematic review study identified 52 risk factors for gastric cancer and were separated into nine groups:

4.2.1 Diet

Diet and eating habits are one of the most important factors in the incidence of gastric cancer. Based on the results, one of the risk factors of the diet mentioned in more studies (compared to other factors) was a salty diet, reported in eight studies. Studies have shown that excessive consumption could act as a stimulant of the gastric mucosa, leading to atrophic gastritis, increased DNA synthesis and cell

proliferation, thus providing the basis for the incidence of gastric cancer. Evidence from previous studies showed that excessive salt intake was associated with risk of gastric cancer. Estimates suggested that 24% of gastric cancer cases in the UK (31% in men and 12% in women) were associated with more than 6 grams of salt per day.

Lack of intake or inadequate intake of fresh fruits and vegetables is another risk factor for gastric cancer (reported in six studies). There are also reports that low intake of fresh fruits and vegetables is a risk factor for gastric cancer. On the other hand, high intake of fruits and vegetables is associated with a reduced risk of gastric cancer (reported in 9 studies). In addition, the results of the meta-analysis of 22 cohort and case-control studies indicated that the consumption of fresh vegetables reduced the risk of gastric cancer (Kim et al., 2010).

On the other hand, a cohort study showed that the risk of gastric cancer was lower in vegetarians than in people who consume meat. Excessive consumption of red meat, smoked meat, processed meat and salted meat have also been reported as other risk factors for this cancer (mentioned in 8 studies). Several mechanisms can result in the production of carcinogenic compounds, such as heterocyclic amines, N-nitrous compounds and polycyclic aromatic hydrocarbons, produced during cooking or due to endogenous reactions.

4.2.2 Lifestyle

In this study, 12 studies pointed out the role of smoking in the risk of gastric cancer. Smoking has devastating and irreversible effects on gastric tissue, which increases the risk of malignancy. This agent is also known as a risk factor for gastric cancer by the International Agency for Research on Cancer (IACR, 2017). Estimates showed that 22% of gastric cancer cases in the UK were related to smoking showed in their case control studies that the case group (patients) smoked significantly more than the control group. Alcoholic beverages are another risk factor reported in 7 studies.

In a meta-analysis, they found that alcohol consumption could increase the risk of gastric cancer (OR) of 1.39). On the other hand, another study reported a link between the risk of gastric cancer and alcohol consumption only in heavy consumption (≥ 4 drinks per day). In addition, the results of Bagnardi's study showed that people who consume + 50g of alcohol per day have a 24% higher risk of gastric cancer compared to other people (who do not consume alcohol or consume less). With regard to the effect of alcohol, it can be said that alcohol creates a cancer-stimulating mechanism that involves a chronic inflammatory response to the toxic effects of ethanol metabolites and cytokines and, therefore, increased nitrosamine intake.

4.2.3 Genetics

The genetic field that refers to a person's characteristics at the genome level is one of the causes of human cancers. The main components of the genetic field are mutations and polymorphisms that affect by

altering the amount of expression or altering the function of proteins. On the other hand, the genetic differences of individuals in each population are the main factors that determine susceptibility to various diseases, from infectious and contagious diseases to non-communicable diseases, such as cancer. When studying genetic factors that cause cancer, the focus is on mutations; however, no specific mutation is known to predispose cancer to all types of cancer. In addition, due to the multivariate nature of cancer, there is a probability of the effect of genetic polymorphisms (the factor of individual differences in susceptibility to disease and response to drug therapy), along with other environmental and genetic factors in the sensitivity of individuals to their incidence. In the present study, 13 studies pointed out the role of genetic factors in the incidence of cancer. To date, a relationship has been identified between gastric cancer and the various polymorphisms of cytokine genes that are the agents of the immune system. Results of a meta-analysis on the correlation between cytokine gene polymorphisms and the risk of precancerous lesions suggested that some of them, such as IL1RNVNTR gene polymorphism, were associated with the risk of these lesions. The results of a study revealed that the genetic polymorphism of CYP19A1, especially rs1004982 rs16964228 and rs1902580, was associated with an increased risk of gastric cancer. In addition, research has shown in its study that genetic polymorphisms of the phenotype CYPE1, NAT2 M1, NAT2 and XRCC1 194 were significantly associated with gastric cancer.

4.2.4 Family history

In this study, eight studies identified the family history of tumors and gastric cancer as a risk factor for gastric cancer; it can provide valuable information about the molecular genetic pathways of cancer and improve our understanding of the gastric carcinogenesis process. In this sense, another study pointed out the first evidence of the effect of the family and inheritance on the incidence of gastric cancer. As reported in their study, the prevalence of gastric cancer was higher in people whose blood relatives (first-degree relatives) had stomach cancer. In addition, another study showed that family history of gastric cancer, especially in first-degree relatives, increased the risk of gastric cancer. Similarly, it has been reported that the risk of gastric cancer in people with a family history of this disease was 2-10 times higher than that of other people.

4.2.5 Infections

Infections including Helicobacter Pylori (alone or in combination with other factors, such as some genetic factors, etc.) and the potential role of human papilloma virus are emerging risk factors. In addition, the human papilloma virus is causally related to tumorigenesis in various types of cancer. The results of a meta-analysis showed that the human papilloma virus could play a potential role in the pathogenesis of gastric cancer.

4.2.6 Demographic characteristics

In one study, age was positively associated with the risk of gastric cancer (cardial and non-cardial). Similarly, in two studies, the case group (patients) was significantly older than the control group. In addition, the gender factor may also play a role in the biology of gastric cancer. Results of a study conducted by Tran et al. showed that males were positively associated with cardiac and non-cardiac cancers. In one study they concluded that men were more likely to be exposed to proximal gastric cancer compared to women. In addition, in one report, standardized rates for the age of stomach cancer were twice as high in men than in women (12.8% and 5.7%, respectively).

Socioeconomic (income) and social (education level) status are other risk factors reported in 10 studies. Income and education, which are the most important determinants of the social class, are directly related to the level of health. This suggests that social class has an impact on health. Many cancers are the result of environmental factors; socioeconomic status is one of the most important determinants of human health and, for most people, health status is mainly determined by the rate of socioeconomic progress. Other studies found that there was an inverse relationship between cancer incidence and social class. Regarding gastric cancer, although socioeconomic status alone may not be associated with the risk of this cancer, it may still be associated with some of its risk factors, including Helicobacter Pylori, and may indirectly play a role in the incidence of this cancer. In a study in Iran, the higher incidence of gastric cancer was associated with lower annual income, lower annual spending on food, fruits and vegetables, higher unemployment rates, and higher percentage of employment in the agricultural and construction sectors. Similarly, the findings of studies showed that the case group (patients) had a significantly lower level of education than the control group. The results of a meta-analysis suggested that the risk of gastric cancer was higher in people with lower socioeconomic status, while another meta-analysis showed that high level of education was associated with a modest decrease in gastric cancer rate.

4.2.7 Occupational Exposure

One of the important factors that determine the health of people in the community is occupational and occupational exposure. In this study, two studies pointed out the impact of occupational exposure on the increased risk of gastric cancer. In their study on the risk factors of occupational and socioeconomic factors, they showed that manual workers and farmers were at higher risk of gastric cancer; cement and mineral dust were considered the most important occupational risk factors for gastric cancer. Similarly, the results of one study showed that the risk of gastric cancer in people with occupational exposure to chromium was 27% higher than in others. In addition, a UK report showed that about 3% of gastric cancer cases in men and 0.3% in women were related to occupational exposure, referring to other occupational risk factors such as carpenters, steel workers and tin miners. However, further studies are needed to examine the role of occupational exposure in the development and incidence of gastric cancer.

4.2.8 Ionizing radiation

Ionizing radiation is another likely risk factor for gastric cancer mentioned in one study. Among radiation, gamma radiation may play a potential role in the development of gastric cancer, with around 1% of reported cases of gastric cancer in the UK associated with radiation. In other research they concluded that increased sensitivity to gamma rejection was associated with an increased risk of gastric cancer; people who were more sensitive to gamma radiation were at higher risk of gastric cancer.

Gastric cancer is one of the multifactorial cancers, and many factors can play a role in its incidence. In the present study, several environmental and genetic factors were identified in the incidence of this cancer. It is suggested that health policy policymakers take appropriate measures to prevent and reduce the burden of gastric cancer in order to improve nutrition and lifestyle and promote community education and awareness. With regard to the immutable nature of some risk factors, screening programs seem necessary for susceptible and at-risk people. Finally, despite the many gaps in the causes and risks of gastric cancer, studies with an appropriate design are needed to address some of the risk factors that can interfere with gastric cancer. [15th]

5 CLINICAL PICTURE AND DIAGNOSIS

Most patients with malignant gastric neoplasia are asymptomatic in around 80% of affected individuals, or present nonspecific symptoms in early stages, becoming evident in more advanced stages. The clinical picture of gastric cancer is usually characterized mainly by weight loss and epigastric pain, which can be confused with peptic [ulcer,10 but] which nevertheless does not improve with feeding or the use of antacids. [2 In] addition to these, there are other symptoms that may also be present according to the location of the tumor.

Tumors in the cardia or gastroesophageal junction region are usually accompanied by dysphagia, and tumors located in the pyloric den typically present symptoms such as vomiting and obstruction of gastric outlet. Signs such as anemia, asthena, malaise, weight loss, and gastric distension may suggest a picture of neoplasia. In addition, some more advanced cases may also present gastrointestinal bleeding.

Detailed anamnesis and physical examination may guide the diagnostic hypothesis of gastric cancer and, therefore, establish a better orientation for the complementary tests necessary for the confirmation of the diagnosis. [16th]

Physical examination in the early stages hardly presents alterations in most cases of gastric cancer, which hinders early diagnosis. In more advanced states, caquechtic patients with a palpable mass in the epigastric region are observed, in addition to reported weight loss and gastric distension.

Other signs are noted in case of metastasis as hepatomegaly with jaundice and ascites in cases of metastasis to the liver, Virchow nodule when there is involvement of supraclavicular lymph node or sister Maria José's nodule when periumbilical lymph node, Krukenberg tumor when there is metastasis to ovaries and splenomegaly to reach portal and splenic veins. In addition, acanthosis nigricans, Trousseau syndrome

(migratory phlebitis) and neuromyopathy are among the paraneoplastic syndromes that may appear in the course of or precede gastric neoplasia. [2.15]

Upper digestive endoscopy is the most specific and sensitive method for the diagnosis of gastric cancer, and detects, when performed with biopsy and cytology, more than 90% of cases of gastric malignancy. Tumor staging, extension and location can also be established from endoscopy. [2] In addition, early detection of gastric neoplasia has become increasingly frequent with the increase in the performance of this procedure.

Moreover, in cases of diagnosis of gastric neoplasia, upper digestive endoscopy is also a useful tool for establishing therapeutic methods from TNM staging, and for evaluating the histological type and tumor response to treatment. [16th]

Gastric tumors may present in the form of ulcers, masses or polyps. Despite the possibility of identifying the malignancy of gastric ulcers by means of upper digestive endoscopy, biopsy and cytology are mandatory whenever there is the presence of lesion. Usually benign lesions have regular and smooth base, while malignant lesions present with irregularities.

Other tests may complement the diagnosis performed by upper digestive endoscopy with biopsy and cytology. Computed tomography of the chest and abdomen allows the evaluation of lymphadenopathy and metastasis to other organs. [2] Abdominal CT shows tumor size and location, as well as nodal, vascular, or visceral tumor involvement.

In addition, endoscopic ultrasound should be performed as diagnostic complementation, which allows better evaluation for tumor invasion and extension, being a tool used for better accuracy of staging. USE is also effective in assessing local lymph node involvement and is ineffective in reaching distant lymph nodes. Therefore, the combination of computed tomography with endoscopic ultrasound is the best choice to evaluate the staging, location and number of lymph nodes involved in gastric neoplasia. [16th]

6 GASTRIC CANCER TREATMENTS

As a type of treatment, surgery (open or endoscopic), chemotherapy, target therapy and radiotherapy or even a combination of them can be listed. The choice of treatment will depend on several factors such as age of the patient, chances of cure, general state of health. However, the main determining factor is the staging of the disease at the time of diagnosis.

Stage 0: Can be treated only with surgery. Total or subtotal gastrectomy, with removal of regional lymph nodes or through endoscopic resection of the mucosa.

Stage I:

Stage IA. They have the tumor and lymph nodes removed by total or subtotal gastrectomy. For some types of cancer at this stage, rarely, endoscopic mucosal resection may be a treatment option.

Stage IB. The main treatment for this stage is total or subtotal gastrectomy. Chemotherapy or chemoiriradiation may be given prior to surgery to reduce tumor size and facilitate surgery. It can be recommended after surgery as well.

Stage II: The main treatment is surgery for total or partial removal of the stomach, omentum and nearby lymph nodes. Many patients are treated with chemoirradiation or chemotherapy prior to surgery to reduce tumor size and facilitate surgical removal. Treatment after surgery may include chemotherapy alone or chemoirradiation.

Stage III: Surgery is the main treatment for patients at this stage, unless the patient is very weak for other clinical reasons. Some patients may be cured with surgery along with other treatments, while for others surgery only helps to control the disease or relieve symptoms. Some patients may undergo chemotherapy or chemoirradiation prior to surgery to reduce tumor size and facilitate surgical removal. Patients who undergo chemotherapy before surgery will probably also do so after surgery.

Stage IV: Healing is usually not possible. Treatment aims to keep the disease under control and relieve symptoms. This may include surgery, such as a gastric bypass or even a subtotal gastrectomy. In some cases, a beam of laser beams directed through an endoscope can destroy most of the tumor and relieve obstruction without surgery. Chemotherapy and/or radiotherapy can often help but cure the disease is not expected. Combinations of chemotherapy drugs are most commonly used, but it is still unclear which combination is best. Target therapy may also be useful in the treatment of advanced cancers.

Relapse: Treatment options for a relapse are usually the same as stage IV. But they also depend on the site of relapse, previous treatments, and the patient's overall health status.

Clinical studies or new treatments may be an option and should always be considered. [17.18]

7 DEFINITION AND TREATMENT OF EARLY CANCER

7.1 DEFINITION OF EARLY GASTRIC CANCER

First described in 1939 by Gutmann, early gastric cancer (CGP) is characterized as malignant gastric neoplasia whose growth is limited to the mucosa (intramucous carcinoma) or submucosal (submucous carcinoma) of the stomach, with or without metastases in regional lymph nodes, according to the definition of the Japanese Digestive Endoscopy Society in 1962[19,20]. It is also called incipient gastric cancer, preinvasive or in situ. Currently, according to the latest TNM[21] classification of stomach cancer of the American Joint Committee on Cancer (AJCC), those lesions entitled T1, whatever the status N and its histopathological subtype, are called CGP.

7.2 TREATMENT

There are several surgical treatments of CGP, such as open surgery (gastrectomy with lymphadenectomy D1 or D2), laparoscopy or endoscopic resection.

Gastrectomy remains, overall, the most used method in the treatment of patients with GPC. It is indicated for patients who do not meet criteria for endoscopic resection or when there is no adequate infrastructure and/or human capital for its performance. Patients who do not fit the indications for endoscopic treatment are at higher risk of lymph node metastases and should be referred for surgery, either openly or otherwise less invasive (laparoscopic or robotic). It is used as the main method of treatment of CGP because it achieves adequate cancer treatment through wide resection margins and lymphadenectomy. However, this modality has considerable rates of perioperative morbidities that compromise the long-term gastrointestinal functions, as well as the quality of life of patients. [10th]

Several authors propose laparoscopy surgery as the gold standard in the treatment of CGP, with results comparable to open surgery. Despite technological advances, laparoscopy is still a challenging procedure for cancer treatment, due to the inherent difficulties of this modality.

The therapeutic alternative for CGP with low risk of lymph node metastasis has been endoscopic resection. Currently, endoscopic treatment of PPC is indicated for patients with moderate or well differentiated intramucous adenocarcinoma , elevated and less than 2cm in diameter or depressed and less than 1 cm without ulceration. However, unnecessary surgeries are likely to be performed, since the criterion of absolute indication is rigorous. Thus, expanded criteria for endoscopic resection have been suggested and many good results have been reported. As proposed by Gotoda et al. (2007): (1) mucosal cancer without ulcer findings, regardless of tumor size; (2) mucosal cancer with ulcer ≤ 3cm in diameter; and (3) minimal submucous invasive cancer (≤ 500 μm of mucosal muscle) with size ≤ 3 cm. [17th]

Common endoscopic modalities include endoscopic mucosal resection (EMR) and endoscopic submucosal dissection (ESD). The ESD technique is currently a more acceptable endoscopic approach for the treatment of CGP without lymph node metastasis compared to RMS. In The ESD, benign (premalignant) and noninvasive malignant neoplastic lesions are resection, in addition to the advantages of greater curative resection and histologically complete resection rate, as well as a lower local recurrence rate for GGP, which were confirmed by large-scale clinical studies and meta-analyses. [17.18]

The endoscopic procedure compared to surgical resection tends to show advantages: low invasiveness, lower cost, better postoperative recovery, lower impairment of gastrointestinal function in the long term and a better quality of life.

8 JUSTIFICATION AND PURPOSE

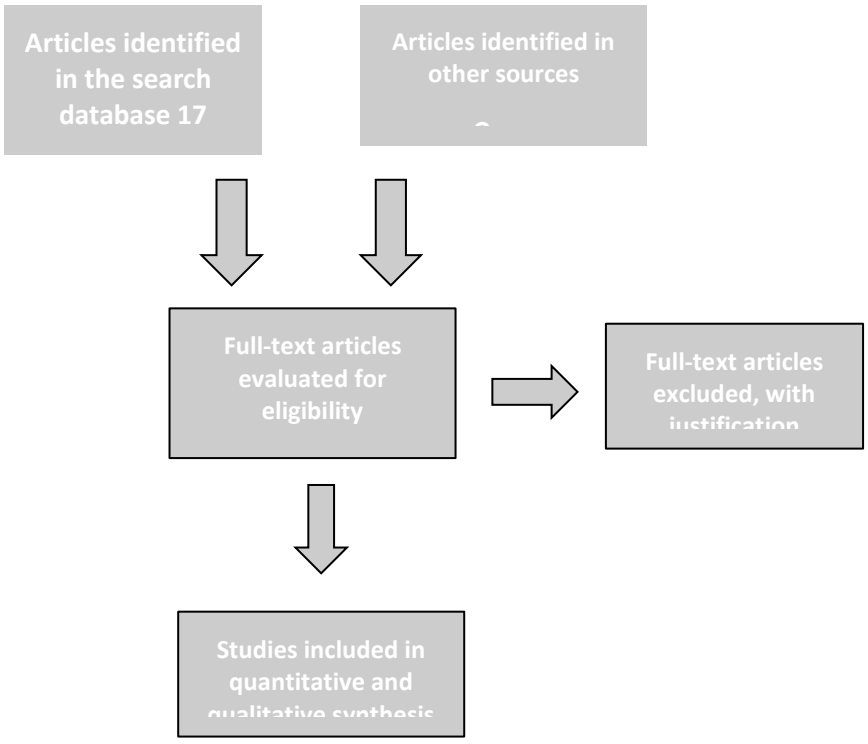
The role of submucosal endoscopic dissection (ESD) in the treatment of GCS is not well established. Clinical parameter visits or outcomes between ESD and GCS resection surgery are still scarce and controversial, and long-term results in patients with sufficient follow-up who have undergone ESD or surgery remain uncertain. Previous meta-analyses comparing ESD with surgery for GCS are scarce and are not robust to reach definitive conclusions. Therefore, the aim of the study is to report a horizontal review that comcants, between ESD and resection surgery, overall survival, adverse event rate, risk rate,

recurrence rate, hospital stay, cost of procedure, age, gender and ethnicity of patients, in addition to data on H's research. Pylori. This study adds an important value to the scientific literature, because it establishes and unifies data on this comparison.

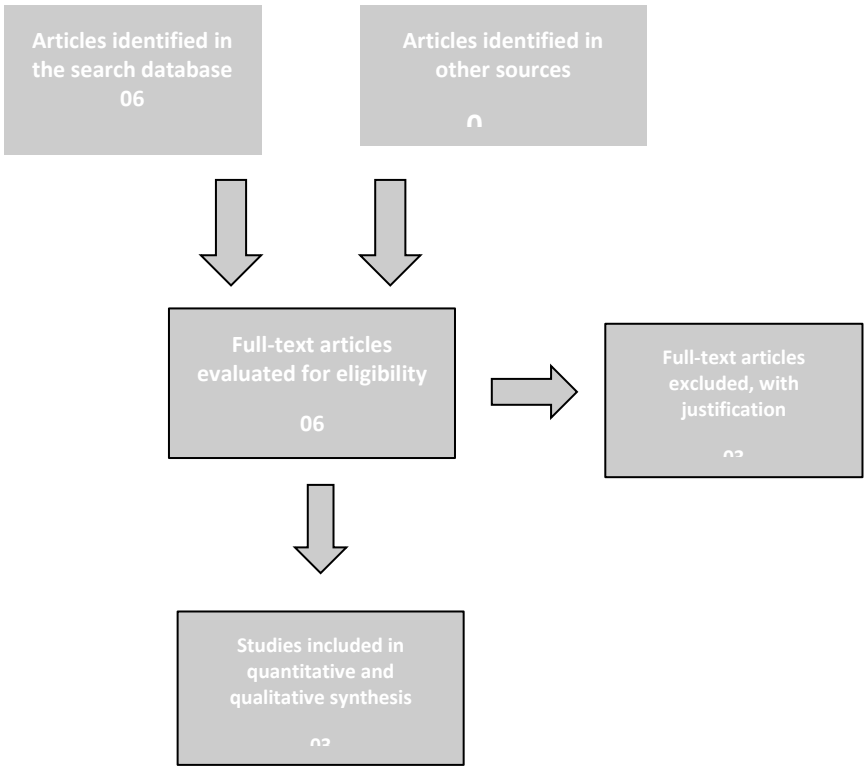
9 METHODS

We performed and reported this horizontal review following the PRISMA method (18). A bibliographic research was carried out in the Pubmed Central databases to identify eligible articles comparing submucosal endoscopic dissection (ESD) with gastrectomy in the treatment of CGP.

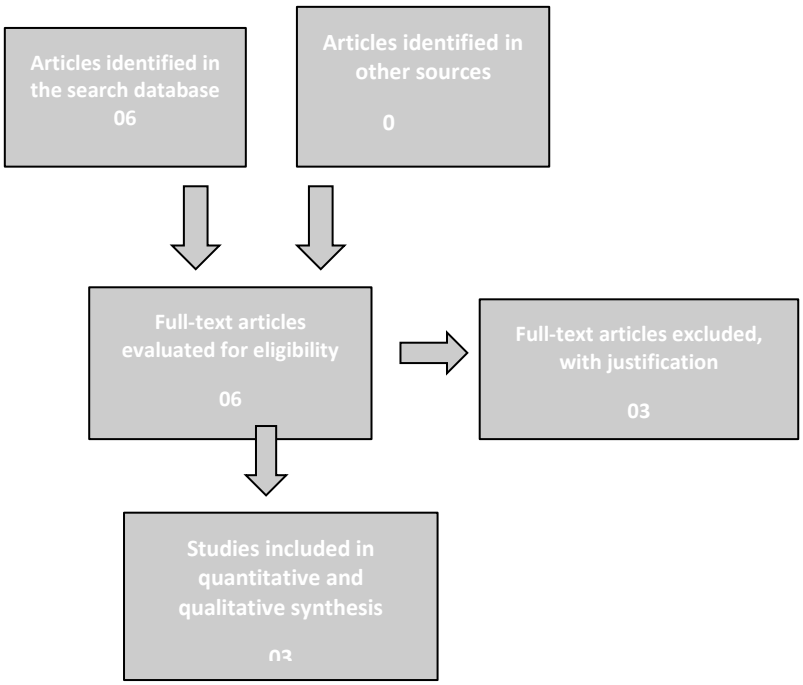
Reviewer 1 searched the search terms "comparison" or "compared" and "ESD" or "submucosal endoscopic dissection" or "EMR" or " endoscopic resection" and "surgery" or "gastrectomy" or "surgical resection" and "early gastric cancer" or "EGC" or "initial stomach cancer". Of the 17 results, 6 were used for the research, in addition to 9 others that were sought from the reference bibliographies of eligible studies and review articles. There was no language restriction in the bibliographic research. Clinical studies published before May 2020 were researched. We then read the full text and determined the eligible studies including a number of 13 articles for that study.



Reviewer 2 searched the PubMed database for articles that included the keywords "early gastric cancer", "treatment", "surgery" and "endoscopic" and filtered for articles published between 2014 and 2020, obtaining 6 results. Of these 3 were chosen and added to the work.

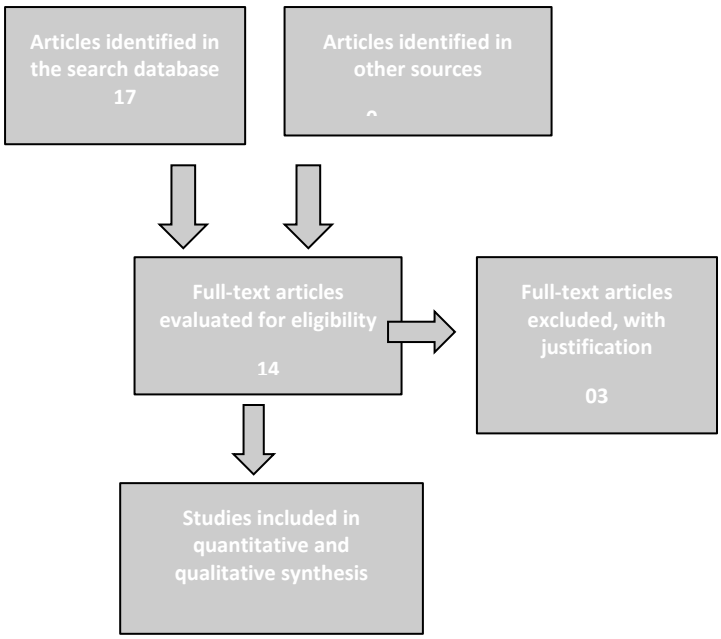


Reviewer 3 searched Pubmed with the key words: "early gastric cancer endoscopic vs cirurgical", on June 13, 2020, 6 results were obtained. Of these six results, only 3 were eligible for the study, because the others did not fit the theme according to the reading of the abstracts of each one.

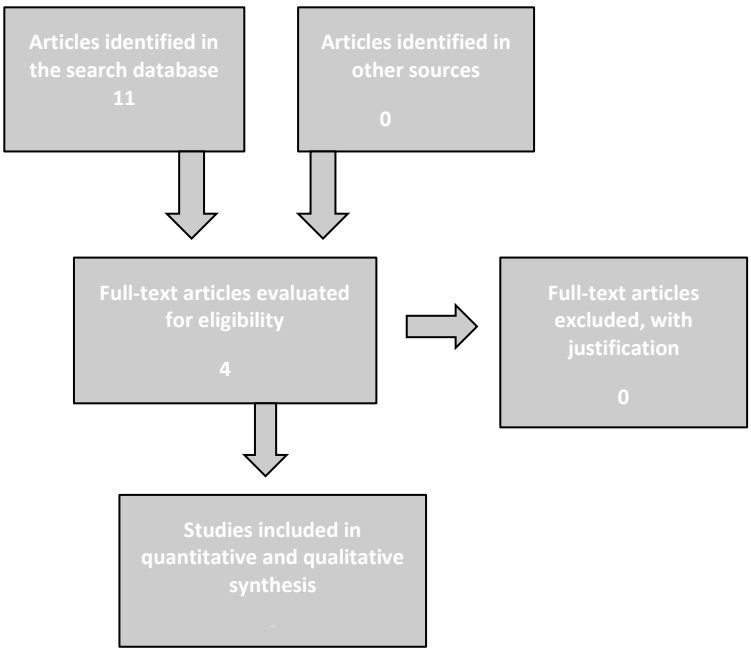


Reviewer 4 searched the PubMed database using the keywords "stomach physiology" and "stomach secretion" for introduction and used 3 of them. We also researched the keywords "endoscopic vs surgical treatment for early gastric cancer", 14 articles were obtained, of which 2 were discarded because they were

in Chinese, 1 was also discarded because it was not relevant and 5 others had already been chosen by the senior reviewer by other reviewers.

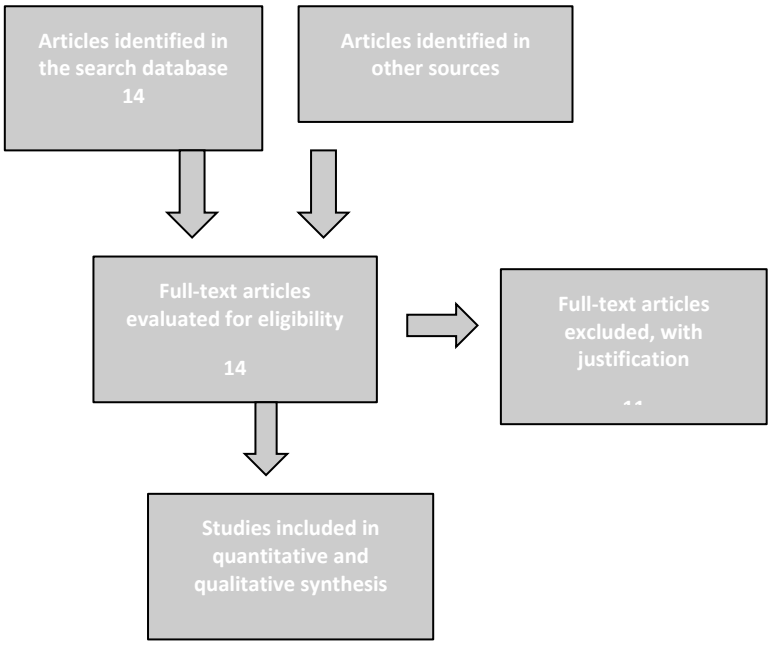


Reviewer 5 searched the PubMed database on May 17, 2020, using the keywords "comparable" or "comparison" followed by the terms "endoscopic vs surgery", "treatment" and "early gastric cancer" ", with the filter for articles published between 2014 and 2020. With this, 54 results emerged, of which only 11 abstracts were analyzed, and of these, only 4 were selected for relevance and eligibility criteria.



Reviewer 6 searched the PubMed database for articles comparating gastrectomy and endoscopic treatment for early gastric cancer. For this, he searched for "Early gastric cancer endoscopic vs surgery". It

was then filtered to show only results from the years 2014 to 2020. In addition, it was filtered only to show reviews, systematic reviews and meta-analyses. With this, there were 14 articles as a result of the research. Of these 14, only 3 were related to the theme of this work.



In total, 36 articles were selected and after final review, 19 of these articles met inclusion criteria.

9.1 FINDINGS

Job name	Year	Author	Type of Work	Number of cases	Number of articles	Study objective	Result
Comparable Cancer-Specific Mortality of Patients With Early Gastric Cancer Treated With Endoscopic Therapy vs Surgical Resection	2020	MirMilad Khoshknab Pourmousavi, Rui Wang, Tossapol Kerdsirichairat, Ayesha Kamal, Venkata S Akshintala, Gulara Hajiyeva, Chawin Lopimpisut, Yuri Hanada, Vivek Kumbhari, Vikesh Singh, Mouen A	Analysis of a population database (Epidemiology of Surveillance and Final Results)	Endoscopic (n = 786) or surgery (n = 2577)		The aim of the study was to evaluate the long-term results after TS compared to surgery in patients with superficial GCS using population-based and to evaluate the trends of endoscopic treatment for superficial GCS in the USA.	The use of endoscopic therapy increased from 15.1% of cases in 1998-2000 to 39.0% of cases in 2013-2014. Endoscopic therapy has been used more frequently in elderly, female or Caucasian patients or with localised lesions in the proximal or with limited depth (Tis vs T1a) and size, compared to surgery. The mean follow-up time was 59 months (interquartile

		Khashab, Olaya Gutierrez Brewer, Eun Ji Shin, Marcia I Canto, Anne Marie Lennon, Saowanee Ngamruengphong					interval, 31-102 months). months). The percentages of overall survival at five years and the specific survival of cancer were 57% and 99% in the endoscopic therapy group and 76% and 95% in the surgery group. After us adjusted for clinical factors using a multivariate model of cox proportional risks, they found no significant difference in specific mortality from gastric cancer among patients who received endoscopic therapy versus surgery (risk rate, 1.42; CI 95%, 0.91-2.23; P = 0.12)
Comparison of Long-Term Outcomes of Endoscopic Submucosal Dissection and Surgery for Early Gastric Cancer: a Systematic Review and Meta-analysis.	2019	Lihu Gu, Parikshit A Khadaroo, Liangliang Chen, Xinlong Li, Hepan Zhu, Xin Zhong, Junhai Pan, Manman Chen	Meta-analysis	4986	13	This study was conducted to investigate the long-term results of endoscopic submucosal dissection, which include overall survival (OS), disease-free survival (DFS), and recurrence rate	The difference in overall survival and specific disease survival between endoscopic submucosal dissection and surgical treatment was not statistically significant. However, disease-free survival in the endoscopy group was much lower than in the surgery group In terms of treatment after recurrence, the proportion of patients who could receive radical treatment was significantly higher in endoscopy than in gastrectomy.
Long-term clinical outcomes of endoscopic vs. surgical resection for early gastric cancer with undifferentiated histology	2019	Lim JH, Kim J, Kim SG, Chung H.	Systematic review of medical records	1147 (126 endoscopy and 1021 by surgery)		This study was designed to compare long-term results between ESD and surgery in the EGC UD, particularly within expanded criteria, to reassess the validity of ESD in The EGC UD	ESD has been demonstrated as a comparable surgical treatment modality for expanding UD EGC criteria, as well as in the EGC differentiated in terms of long-term effectiveness. However, the current expanded criteria seem to be likely to lose

							occult lymph node metastases and induce unfavorable outcome. Therefore, limiting the indication up to 1 cm in the size criteria, in addition to excluding mucinous adenocarcinoma may be appropriate to avoid the risk of recurrence. In addition, meticulous endoscopy of regular surveillance after ESD should be followed for possible metachronic tumor development.
Propensity Score-Matched Comparison of Short-Term and Long-Term Outcomes Between Endoscopic Submucosal Dissection and Surgery for Treatment of Early Gastric Cancer in a Western Setting	2019	Bausys R, A Bausys, J Stanaitis, I Vysniauskaite, K Maneikis, B Bausys, E Stratilatovas, K Strupas	Retrospective control case study	260		This study aimed to compare the short- and long-term results of ESD and surgery for GCS	Of the 260 eligible patients, 42 (16.1%) underwent SDS. After the correspondence, two well-balanced groups were analyzed, consisting of 42 patients in each. The time of operation (83 vs. 151 min., P = 0.001) and postoperative hospitalization (5.4 vs. 13.4 days, p = 0.001) were significantly lower in the group with SSD. The five-year survival rate was significantly higher in the surgery group (97.6% vs. 77.5%, p = 0.002). However, this difference was reduced after excluding cases of non-curative SDS (97.6% vs. 89.7%, p = 0.099). There was no significant difference in the 5-year S g rate between the study groups (73.8% vs. 69.0%, p = 0.599)
Comparison of endoscopic submucosal dissection with surgical gastrectomy for early gastric cancer: An updated	2019	Hua Li, Li-Qian Feng, Yao-Yao Bian, Li-Li Yang, Deng-Xiang Liu, Zhi-Bin Huo, Li Zeng	Goal-analysis	5112	4	Toimprove the safety and efficacy in the short and long term among the results of endoscopic vs surgical treatment	The results of the meta-analysis demonstrated some advantages of the endoscopic procedure, such as decreased operative time, shorter hospital stay and lower rates of postoperative complications. However, patients undergoing endoscopic treatment have higher

meta-analysis.							recurrence rates than patients undergoing surgery.
Long-Term Outcomes Comparison of Endoscopic Resection With Gastrectomy for Treatment of Early Gastric Cancer: A Systematic Review and Meta-Analysis.	2019	Liangliang An, Sharen Gaowa, Haidong Cheng, Mingxing Hou	Systematic and meta-review analysis	2432	9	Compare long-term results of endoscopic resection with gastrectomy for early gastric cancer treatment	Endoscopic resection was associated with a shorter hospitalization period and lower rates of postoperative complications when compared to gastrectomy. However, the recurrence rate was higher in endoscopic resection, mainly due to metastases. However, most of these tumors could be treated again with endoscopic treatment, and this did not affect the overall survival of patients with early gastric cancer. There was no difference in the overall survival rate between endoscopic resection and gastrectomy.
Updated Evaluation of Endoscopic Submucosal Dissection Versus Surgery for Early Gastric Cancer: A Systematic Review and Meta-Analysis	2019	Qing Liu, Li Ding, Xiewu Qiu, Fanjie Meng	Systematic and meta-review analysis	5993	18	Compare endoscopic submucosal dissection vs surgery in the treatment of early gastric cancer.	The ESD procedure has a marked advantage over surgical treatment, in terms of shorter operating time. Deaths related to the procedure only occurred in the group submitted to surgery. The total number of adverse events was lower in the group submitted to ESD, as well as shorter hospital stay, less trauma, and better quality of life. In addition, the ESD proved to be a cheaper procedure. The most common complications in patients undergoing ESD are perforation and bleeding. However, in most cases, these complications can be resolved through endoscopic treatment. As reported in other meta-analyses, the study concludes that the risk of recurrence is higher in the ESD group.

The Comparison Between Endoscopic Submucosal Dissection and Surgery in Gastric Cancer: A Systematic Review and Meta-Analysis	2018	Junbi Hu, Yan Zhao, Mudan Ren, Yarui Li, Xinlan Lu, Guifang Lu, Dan Zhang, Dake Chu, and Shuixiang He	Systematic review and meta-analysis	2016	13	The data sought were to compare complications related to perforation and bleeding, synchronous cancer, metachronic cancer, complete resection, adverse events, hospitalization, hospital cost, quality of life, disease-free survival rate (LST) at 5 years and survival rate at 3 years.	The incidence of perforation in two groups was different [OR = 6.18 (95% CI: 1.37–27.98), *P* = 0.02]. The prevalence of synchronous and metachronic cancer in the SSD group was higher than those of the surgery group [OR = 8.52 (95% CI: 1.99-36.56), *P* = 0.004 and OR = 7.15 (95% CI: 2.95–17.32), *P* <0.0001]. Recurrence and complete resection rates were different [OR = 6.93 (95% CI: 2.83-16.96), *P* <0.0001 and OR = 0.32 (95% CI: 0.20-0.52), *P* <0.00001]. Compared to the surgery group, the length of hospital stay was shorter [IV = -7.15 (95% CI: -9.08-5.22), *P*<0.00001], the rate of adverse events was lower and quality of life (QOL) was better in the SSD group. The bleeding difference was not found.
Comparison of Clinical Outcomes After Endoscopic Submucosal Dissection and Surgery in the Treatment of Early Gastric Cancer: A Single-Institute Study	2017	Ji Young Chang, Ki-Nam Shim, Chung Hyun Tae, Ko Eun Lee, Jihyun Lee, Kang Hoon Lee, Chang Mo Moon, Seong-Eun Kim, Hye-Kyung Jung, Sung-Ae Jung, Joo-Ho Lee, Min-Sun Cho	Single clinical study	159		Investigar whether the adverse outcomes or events associated with endoscopic dissection of the submucosa are comparable to those of surgery for early gastric cancer, including absolute and expanded indications	The group of endoscopic submucosal dissection and surgery showed no significant difference in the incidence of residual disease (*P* = 0.48), local recurrence (*P* = 0.46) and metachronic cancer (*P* = 0.22). Kaplan – Meier's analysis showed no significant difference in the overall survival rate at 2 years (97.6% versus [vs] 92.4%; *P* = 0.45) and 5 years (95.8% vs 95.6%; *P* = 0.26) between 2 groups. There was also no significant difference in the disease-free survival rate at 2 years (100% vs. 94.1%; *P* = 0.98) and in 5 years (100% vs 98.4%; *P* = 0.89). Early and late

							adverse events also showed no significant differences.
Endoscopic Resection Versus Radical Gastrectomy for Early Gastric Cancer in Asia: A Meta-Analysis	2017	Fei-Long Ning, Chun-Dong Zhang, Peng Wang, Shuai Shao, Dong-Qiu Dai	Meta-analysis	7983	2355	This article comms on the efficacy and safety of RE and GR (radical gastrectomy) for CGP in Asia.	15 retrospective studies were included in this analysis (3737 patients in the ER group and 4,246 patients in the RG group). No significant differences were observed in the three-year survival rate (OR, 0.87; 95% CI, 0.50-1.53) and five-year survival rate (OR, 0.81; CI 95%, 0.58-1.13) between the ER and RG groups. . Although patients submitted to RE had a higher risk of recurrence (OR, 6.07; 95% CI 4.17-8.84) and metachronic cancer occurrence (OR, 8.35; 95% CI, 5.48-12.75), recurrent or metachronic gastric cancers after RE were successfully detected and removed by endoscopic technique. Higher recurrence in the ER group may be associated with lower block resection rate (OR, 0.05; CI95%, 0.02-0.14) and complete resection rate (OR, 0.03; IC95%, 0.01-0.08). It is important to highlight that, although three-year survival and five-year survival were similar in both groups, the rate of complications in the ER group was significantly lower than in the RG group
Long-Term Outcome of Endoscopic Vs. Resection Surgery for Early Gastric Cancer: A Non-	2016	Jeung Hui Pyo, Hyuk Lee, Byung-Hoon Min, Jun Haeng Lee, Min Gew Choi, Jun Ho Lee, Tae Sung Sohn, Jae	Prospective review	Endoscopic resection (1,290 patients) and surgery (1,273 patients) for GCS.		The aim of this study was to compare the long-term results of endoscopic resection with those of surgery for early gastric cancer (GCS).	In a propensity analysis of 611 pairs, the proportion of 10-year OS was 96.7% in the endoscopic resection group and 94.9% in the surgery group (P = 0.120) (risk difference -1.8%, 95% confidence interval (CI) -4.04-

inferiority-Matched Cohort Study		Moon Bae, Kyung-Mee Kim, Joon g Hyun Ahn, Keumhee C Carriere, Jae J Kim, Sung Kim					0.44, lower than Pnon = 0.014), which met the criterion of non-inferiority. On the other hand, the proportion of RFS at 10 years was 93.5% in the endoscopic resection group and 98.2% in the surgery group (P <0.001) (risk difference 4.7%, 95% CI 2.50-6.97, Pnon inferiority = 0.820), which did not meet the criterion of non-inferiority, mainly due to metachronic recurrence in the endoscopic resection group. The rate of early complications was higher in the endoscopic resection group than in the surgery group (9.0 vs. 6.6%, P = 0.024), while the rate of late complications was higher in the surgery group than in the endoscopic resection group (0.5 vs. 2.9%, P <0.001). In cox's multiple regression analysis, patient age, comorbidity index, performance index, gender, tumor morphology and depth of invasion were predictors of OS in ECG patients.
Comparison of Endoscopic Resection and Gastrectomy for the Treatment of Early Gastric Cancer: A Meta-Analysis	2016	Fan-Sheng Meng, Zhao-Hong Zhang, Ya-Mei Wang, Lin Lu, Jin-Zhou Zhu, Feng Ji	Meta-analysis	2070	3813	Comnotes the efficacy and safety of endoscopic resection and gastrectomy for patients with early gastric cancer	This meta-analysis involved 10 studies with 2070 patients: 993 patients undergoing endoscopic resection and 1077 who underwent gastrectomy. Endoscopic resection was associated with shorter hospitalization time (standardized mean difference -2.02; 95% confidence interval [CI] -2.64 to -1.39) and lower complication rate (relative risk [RR] 0.41; CI95% 0.22-0.76) than gastrectomy. However,

							endoscopic resection was associated with lower rates of block resection (odds ratio [OR] 0.05; IC95% 0.02-0.16) and histologically complete resection (OR 0.04; CI95% 0.01–0.11) and higher recurrence rates (RR 5.23; CI95% 2.43-11.27) and metachronic cancer (RR 5.22; CI95% 2.40-11.34) than gastrectomy. The overall survival rate (OR 1.18; CI95% 0.76-1.82) was similar.
Endoscopic submucosal dissection versus surgical resection for early gastric cancer: a retrospective multicenter study on immediate and long-term outcome over 5 years	2016	Seung Jee Ryu, Byung-Wook Kim, Boo Gyeong Kim, Ji Hee Kim, Joon Sung Kim, Jin Il Kim, Jae-Myung Park, Jung-Hwan Oh, Tae Ho Kim, Jin-Jo Kim, Seung-Man Park, Cho Hyun Park, Kyo Young Song, Jun Hyun Lee, Sung Geun Kim, Dong Jin Kim, Wook Kim	Multicenter retrospective study	Not informed	Retrospectively analyzed data of patients from 5 centers undergoing ESD or surgical resection	Evaluate the immediate and long-term clinical and oncological results of patients undergoing ESD compared to surgical resection	The study concludes that ESD can be an effective and acceptable treatment for GPC, considering the overall survival rates with fewer complications and shorter hospital stay in relation to the surgical group.
Comparing Laparoscopic to Endoscopic Resections for Early Gastric Cancer in a High Volume North American Center	2016	Sara Najmeh, Jonathan Cools-Lartigue, Carmen Mueller, Lorenzo E Ferri	Retrospective study	155	Cases of a high-volume North American center	The aim of the study was to compare results of endoscopic and surgical resection of malignant and premalignant gastric tumors	The hospital stay was shorter in the ESD group. There was no difference in complication rates in both groups. There was no significant difference between the two groups in terms of overall survival and disease-free survival

Endoscopic Resection Versus Surgery for Early Gastric Cancer: A Systematic Review and Meta-Analysis	2015	Kaiyu Sun Shuling Chen Jinning Ye Hui Wu Jianjun Peng Yulong He Jianbo Xu	Sistemátic review and meta-analysis	1950	9	Andclarify the long-term results and safety of ER and surgery for GCS. Overall survival (OS), recurrence-free survival (RFS) and adverse event rates were investigated	There were no significant differences in relation to SG (TR: 0.995, 95% CI: 0.836-1.185; *P* = 0.959) and rates of adverse events (SG: 0.50, 95% CI: 0.20-1.28, *P* = 0.148) between ERs and gastrectomy . However, patients submitted to RE had significantly lower LRS (Risk rate(TR): 7.226, 95% CI: 1.718-30,400, *P* = 0.007) than those undergoing gastrectomy.
Endoscopic Resection Versus Surgical Resection for Early Gastric Cancer: A Systematic Review and Meta-Analysis	2015	Weili Sun 1, Xiao Han, Wu Siyuan, Yang Chuanhua	Meta-analysis	6118	19	Toprevent the efficacy and safety of endoscopic resection and surgical resection among patients with early gastric cancer.	Endoscopic resection was associated with similar long-term results and considerable advantages over operating time, hospitalization, costs and complications compared to surgical resection, and was also associated with disadvantages such as a higher incidence of local recurrence and metachronic lesions. More high-quality studies from more countries are needed to confirm these results.
Endoscopic Resection Compared with Gastrectomy to Treat Early Gastric Cancer: A Systematic Review and Meta-Analysis	2015	Shuanhu Wang,* Zongbing Zhang, Mulin Liu, Shiqing Li, and Congqiao Jiang	Systematic review and meta-analysis	1466	6	Compara endoscopic resection and gastrectomy for the treatment of early gastric cancer.	The five-year survival rate was similar between endoscopic resection and gastrectomy. Endoscopic resection was associated with shorter hospital stays and reduced overall postoperative morbidity.
Long-term Survival After Endoscopic Resection Versus Surgery in Early	2015	Young-Il Kim, Young-Woo Kim, Il Ju Choi, Chan Gyoo Kim, Jong Yeul Lee, so-Jeong Cho,	Retrospective review	457	Not informed	The aim of the study was to evaluate long-term results of endoscopic resection compared to surgical resection for CGP, with expanded indication criteria	Endoscopic resection may be a great alternative to surgery in cases of GPC that meet expanded indication criteria due to a comparable overall

Gastric Cancers		Bang Wool Eom, Hong Man Yoon, Keun Won Ryu, Myeong-Cheorl Kook					survival rate between the two groups
Endoscopy vs Surgery in the Treatment of Early Gastric Cancer: Systematic Review	2015	André Kondo, Eduardo Guimarães Hourneaux de Moura, Wanderley Marques Bernardo, Osmar Kenji Yagi, Diogo Turiani Hourneaux de Moura, Eduardo Turiani Hourneaux de Moura, José Gonçalves Pereira Bravo, Kendi Yamazaki, Paulo Sakai	Systematic review	2654	11	Establish the short- and long-term outcomes of endoscopic resection compared to surgery in the treatment of CGP	There were no differences in risk after endoscopic and surgical treatments. Survival data after 5 years showed no difference between the two groups. Recurrence rates were analyzed in 5 studies (1331 patients) and there was no difference between approaches. Adverse events were identified in 8 studies (n = 2439). A significant difference was detected demonstrating better results with endoscopy. Mortality data were obtained in 4 studies (n = 1107) and there was no difference between the groups.

Job name	Summary
Endoscopic Resection Versus Surgery for Early Gastric Cancer: A Systematic Review and Meta-Analysis	ABBREVIATIONS: CI confidence interval, REM endoscopic mucosaresection, CGP early gastric cancer, RE Endoscopic resection, DSE endoscopic submucosal dissection, TR risk rate, RHs, risk rates, ORs, odds ratio, General survival SG, Recurrence-free survival SLR **Objectives :Endoscopic resection (RE) is becoming an increasingly widely used treatment option for early gastric cancer (CGP); however, data comparating the long-term results of RE and surgery are limited. In this sense, our objective here was to perform a meta-analysis to clarify the long-term results and safety of RE and surgery for CGP.** Methods: The literature on the direct comparison of RE and surgery for CGP was retrieved from the Medline, PubMed and Scopus databases. The following research chain was used: (ESD) OR (submucosal endoscopic dissection) OR (EMR) OR (endoscopic mucosal resection) OR (ER) OR (endoscopic resection)) AND (surgery OR operation) AND (early gastric cancer)We selected the eligible studies (Inclusion criteria: participants diagnosed histologically with GCS; comparison

	between RE and surgery for CGP; prognosis (survival or recurrence rates) or adverse event rates were examined; and risk rates for death and recurrence and their 95% confidence intervals were extractable; exclusion criteria: animal studies, single case reports, reviews and comments, and studies with insufficient data available for analysis), we extracted the data (author, year of publication, region, sample size, treatment protocols, age and gender distribution, type of study, follow-up and outcome measures, such as GS, recurrence-free survival (SLR) and adverse event rates, as well as data that may affect the evaluation of prognosis: comorbid disease, depth of tumor invasion, histology, tumor size, pre - and postoperative treatments, surgical methods and RE methods, and the combined risk ratio (CR), odds ratio (OR) and 95% confidence interval (CI) were estimated. **Results: Nine retrospective studies were identified, including 973 and 1190 participants undergoing RE and surgery, respectively. There were no significant differences in relation to SG (TR: 0.995, 95% CI: 0.836-1.185; *P* = 0.959) and rates of adverse events (SG: 0.50, 95% CI: 0.20-1.28, *P* = 0.148) between ERs and gastrectomy . However, patients submitted to RE had significantly lower LRS (Risk rate(TR): 7.226, 95% CI: 1.718-30,400, *P* = 0.007) than those undergoing gastrectomy.** **Conclusions: Despite the limitations of this review, including the retrospective nature of all included studies, our results suggest that RE may be a viable and safe treatment strategy compared to gGP gastrectomy; however, careful endoscopic surveillance is required to ensure favorable results. These findings should be confirmed in other large-scale, prospective, randomized and controlled clinical trials from different countries.**
The Comparison Between Endoscopic Submucosal Dissection and Surgery in Gastric Cancer: A Systematic Review and Meta-Analysis	Objectives: There are two treatment modalities for early gastric cancer (CGP) - surgery and endoscopic submucosal dissection (SDRs). Our objective was to compare the safety and efficacy of SD with surgery. Method: A pubmed search was conducted using the terms (ESD OR submucosal submucosal endoscopic dissection) AND (gastric cancer OR gastric carcinoma OR stomach cancer OR intraepithelial neoplasia) AND (operation OR surgery OR surgical resection OR) . Inclusion criteria: only adults were included in the study, only patients diagnosed with GCS were included, regardless of lymph node metastasis, studies definitely included two groups, submucosal endoscopic dissection and surgery groups, and there were no limitations in gastrectomy or laparoscopic resection. articles published in English were included; exclusion criteria: editorials; comments; letters to the editor; review articles; case reports; guidelines articles; animal studies; number of patents in any study included with less than ten; studies including patients with other malignant diseases, such as esophageal carcinoma, colorectal cancer, and polyps; articles without explicit data on the ESD group, but endoscopic resection (ER); and articles with insufficient data. The data sought were to compare complications related to perforation and bleeding, synchronous cancer, metachronic cancer, complete resection, adverse events, hospitalization, hospital cost, quality of life, disease-free survival rate (LST) at 5 years and survival rate at 3 years. The data were extracted using predefined form and odds ratio (OR) with 95% confidence intervals (CI) calculated and *P value.* Results: 13 studies were identified. The incidence of perforation in two groups was different [OR = 6.18 (95% CI: 1.37–27.98), *P* = 0.02]. The prevalence of synchronous and metachronic cancer

	in the SSD group was higher than those of the surgery group [OR = 8.52 (95% CI: 1.99-36.56), *P* = 0.004 and OR = 7.15 (95% CI: 2.95–17.32), *P* <0.0001]. Recurrence and complete resection rates were different [OR = 6.93 (95% CI: 2.83-16.96), *P* <0.0001 and OR = 0.32 (95% CI: 0.20-0.52), *P* <0.00001]. Compared to the surgery group, the length of hospital stay was shorter [IV = -7.15 (95% CI: -9.08-5.22), *P*<0.00001], the rate of adverse events was lower and quality of life (QOL) was better in the SSD group. The bleeding difference was not found. Conclusion: ESD seems to be preferable for GCS due to a lower rate of adverse events, shorter hospitalization time, lower cost and higher QoL.
Comparison of Endoscopic Resection and Gastrectomy for the Treatment of Early Gastric Cancer: A Meta-Analysis	It is a study by Fan-Sheng Meng and et al, published in December 2015. It is a meta analysis that comcants the efficacy and safety of endoscopic resection and gastrectomy for early gastric cancer. The methods used were the electronic research - through pubmed, embase and web of science - of relevant studies comparing the two types of treatment between the years 1976 to March 2015. Inclusion criteria were: patients with pathological diagnosis of early gastric cancer, endoscopic resection compared with gastrectomy, quality index was 5 points or higher, studies that analyzed at least two points including: hospital stay time, block resection rates, complete resection, complications, recurrence, metachronic cancer and overall survival. Exclusion criteria were: comments, reviews, case reports, guidelines, studies with patients without early gastric cancer or with other tumors in other organs and studies with insufficient data. A total of 10 studies with 2,070 patients were included in this meta-analysis, 993 patients treated with endoscopic resection and 1077 patients treated with gastrectomy. The results of this meta-analysis showed that: endoscopic resection is associated with shorter hospital stay and lower complication rates in relation to gastrectomy. However, endoscopic resection is associated with lower rates of block resection, complete histological resection, and higher rates of recurrence and metachronic cancer in relation to gastrectomy. The overall survival rate of these two procedures was similar. The limitations of this meta-analysis were all the studies included were retrospective, with relatively low quality, in addition, these studies showed a significant heterogeneity, most studies were from Japan and South Korea, countries with advanced technology in endoscopy, some of the patients were not selected according to absolute or expanded indications, and some definitions and criteria for the main points of this meta-analysis, some of the patients were not selected according to absolute or expanded indications, and some definitions and criteria for the main points of this meta-analysis, some of the patients were not selected according to the absolute or expanded indications, and some definitions and criteria for the main points of this meta-analysis, some of the patients were not selected according to the absolute or expanded indications, and some definitions and criteria for the main points of this meta-analysis, some of the patients were not selected according to the absolute or expanded indications, and some definitions and criteria for the main points of this meta-analysis differ slightly between studies, which may have influenced the final result. The conclusion of this meta-analysis reveals that endoscopy for the treatment of early gastric cancer is effective as gastrectomy, besides having greater safety and lower cost for patients. A high proportion of patients with early gastric cancer may benefit from endoscopy treatment, making endoscopy a first-line treatment for patients who meet the indicated criteria. Surgery may be an alternative or second-line treatment when endoscopy cannot be curative.

Endoscopic Resection Versus Surgical Resection for Early Gastric Cancer: A Systematic Review and Meta-Analysis	Endoscopic resection (RE) has been widely accepted in the treatment of early gastric cancer (GCS) in place of surgical resection (SR). The objective of this meta-analysis was to perform a comprehensive comparison between the two methods. Four databases in the literature, including PubMed, Web of Science, Cochrane Library and EMBASE, were researched for studies comparators ER with SR to treat GCS. In this meta-analysis, the primary and secondary parameters were compared between the two groups. Primary outcomes included overall survival (OS), disease-specific survival (SSD), disease-free survival (DFS), and recurrence-free survival (RFS). Secondary outcomes included operation-related death, local recurrence, metachronic lesions, procedure-related complication, bleeding, hospitalization, operating time, and cost. Nineteen studies consisting of a total of 6118 patients were identified and selected for evaluation. The meta-analysis showed that the long-term results of RE versus SR for GcS were comparable in terms of 5-year OS (risk ratio [RR] 1.00, 95% [CI] 0.98–1.02), DSS (RR 0.98, 95% CI 0.89-1.08), DFS (RR 0.95, 95% CI 0.86-1.05) and RFS (RR 0.98, 95% CI 0.94-1.01). However, ER had shorter operating time (mean standardized difference [MDS] -3.39, 95% CI -3.58 to 3.20), hospitalization (MDS -2.86, CI 95% -4.02 to -1.69), lower costs (MDS -5.30, 95% CI -10.37 to -0.22) and fewer complications related to the procedure (RR 0.43, 95%CI 0.28-0.65) compared to MR. However, ER had a higher incidence of local recurrence (risk difference 0.01, 95% CI 0.00-0.02) and metachronic lesions (RR 6.81, 95% CI 3.80-12.19). Endoscopic resection was associated with similar long-term results and considerable advantages over operating time, hospitalization, costs and complications compared to SR, and was also associated with disadvantages such as a higher incidence of local recurrence and metachronic lesions. More high-quality studies from more countries are needed to confirm these results.
Endoscopic Resection Compared with Gastrectomy to Treat Early Gastric Cancer: A Systematic Review and Meta-Analysis	Introduction: Endoscopic resection and gastrectomy are treatment modalities for early gastric cancer, but their relative benefits and risks are unclear. We conducted a systematic review and meta-analysis to compare endoscopic resection and gastrectomy for the treatment of early gastric cancer. Methods: We searched PubMed, Embase and Cochrane Library by April 2015 for studies comparing endoscopic resection with gastrectomy for treatment of early gastric cancer. Outcome measures were overall survival (OS) in five years, hospitalization time and postoperative morbidity. We calculated the combined risk ratio (HR), the weighted mean difference (ROM) and the odds ratio (OR) using random effect models. Results: Six studies involving 1,466 patients (618 endoscopic resections and 848 gastrectomy) met the inclusion criteria. Overall survival at five years was similar between endoscopic resection and gastrectomy (HR, 1.06; 95% CI: 0.61 to 1.83). Endoscopic resection was associated with shorter hospital stays (ROM, -6.94; 95% CI: -7.59 to -6.29) and reduction of general postoperative morbidity (OR, 0.36; CI 95%: 0.17 to 0.74). Conclusions: Although overall five-year survival is similar between endoscopic resection and gastrectomy, endoscopic resection offers shorter hospital stay and fewer complications than gastrectomy in the treatment of early gastric cancer. Endoscopic resection is a reasonable treatment for early gastric cancer, with an insignificant risk of lymph node metastasis.
Comparison of Long-Term Outcomes of	Introduction: Submucosal endoscopic dissection (ESD) is an endoscopic alternative to surgical resection of early gastric cancer (GCS). In addition to offering diagnostic and therapeutic capacity, it has the

Endoscopic Submucosal Dissection and Surgery for Early Gastric Cancer: a Systematic Review and Meta-analysis	benefits of reducing postoperative complications and provides rapid recovery and better quality of life compared to surgical resection of neoplastic lesions. However, due to the limitations of the procedure, its long-term results are quite controversial. Methods: This study was conducted to investigate the long-term results of ESD, which include overall survival (OS), disease-free survival (DFS) and recurrence rate. The following databases were used to search for articles published until February 2018: Medline, Cochrane Library, PubMed, Web of Science, and EBSCO. Results: A total of 13 eligible studies, covering 4,986 patients, were selected for a meta-analysis based on the specified inclusion and exclusion criteria. The difference in OS and disease-specific survival (SSD) between SDS and surgical treatment was not statistically significant (RR = 0.90, 95% CI = 0.68-1.19, p = 0.46; RR = 0.40, 95% CI = 0.15-1.03, p = 0.06, respectively). However, DFS in the ESD group was much lower than in the surgery group (RR = 3.40, 95% CI = 2.39-4.84, p <0.001). In terms of treatment after recurrence, the proportion of patients who could receive radical treatment was significantly higher in ESD than in gastrectomy (OR = 5.27, 95% CI = 2.35-11.79, p <0.001). Conclusions: This meta-analysis showed that ESD may be an alternative treatment option to surgery for patients with GCS in Asian countries. However, a rigorous surveillance program is needed after ESD, considering the greater possibility of tumor recurrence after ESD.
Long-term clinical outcomes of endoscopic vs. surgical resection for early gastric cancer with undifferentiated histology	It is a study published in 2018 comparing the long-term efficacy of endoscopic submucosal dissection versus surgical resection for undifferentiated early gastric cancer due to the relatively high risk of lymph node metastasis. The **method** used was a **systematic review** of medical records of patients treated with both endoscopic and surgical dissection between January 2007 and December 2014 at seoul national university hospital (Korea), the comparison was made in relation to survival. The inclusion criteria of the patients were: over 20 years, early gastric cancer, undifferentiated histology including the poorly differentiated, no evidence of lymph node metastasis or distant metastasis by computed tomography and ultrasound endoscopy. The exclusion criteria were; previously treated gastric cancer patients, patients diagnosed with other cancers 5 years before or after the diagnosis of early gastric cancer, patients who were unable to obtain the survival date. The total of 1147 patients, 126 of which were endoscopically treated and 1021 by traditional surgery , **showed** no significant difference between them.
Comparable Cancer-Specific Mortality of Patients With Early Gastric Cancer Treated With Endoscopic Therapy vs Surgical Resection	The method an analysis of a population database to determine the results of patients with gastric cancer of the mucosa undergoing endoscopic therapy versus surgery, the comparison was performed according to the overall survival and specific survival times of gastric cancer after the control of covariates. They used the Surveillance Epidemiology and Final Results database to identify and compare characteristics and outcomes of patients undergoing endoscopic therapy (n = 786) or surgery (n = 2577) for tis or T1aN0M0 superficial gastric cancer, diagnosed between 1998 and 2014. The selected patients were 18 years or older, with histologically confirmed primary gastric cancer, undergoing endoscopic therapy or surgical resection. Patients in stage T1bN0M0, with lymph node metastasis or distance at the time of diagnosis, with follow-up of less than six months and with cancer diagnosed only at the time of autopsy or death certificate were excluded. In the discussion it was observed that over the years there was an increase in endoscopic procedures in relation to surgical treatment, however endoscopic treatment is

	performed mainly in patients of older age due to surgical risks so post-procedure survival is probably slightly lower in this treatment. The greatest limitation of the work is the retrospective , natural observation of the study. The study conclusions found that endoscopic therapy has been increasingly used, however the specific long-term survival for early gastric cancer did not differ among patients undergoing endoscopic and surgical treatment after adjustments for clinical factors.
Long-Term Outcome of Endoscopic Vs. Resection Surgery for Early Gastric Cancer: A Non-inferiority-Matched Cohort Study	It is a large-scale retrospective study comparing the long-term outcome of perioperative morbidity and mortality rates between endoscopic and surgical treatments for early gastric cancer. In order to prove that the endoscopic technique is not inferior to surgical. The study included patients who underwent endoscopic or surgical resection for early gastric cancer at Samsung Medical Center. Data were prospectively collected between January 2002 and December 2012. Inclusion criteria were: over 20 years, recent diagnosis of early gastric cancer without previous treatment and early gastric cancer compatible with endoscopic treatment. Exclusion criteria were: suspicion of lymph node metastasis by endoscopic ultrasound or computed tomography, presence or history of cancer in other organs, and follow-up less than 2 years. To reduce selection bias, they used an analysis with propensity matching between the groups. The results did not demonstrate an inferiority of the endoscopic process in relation to the surgical in 10 survival. However, there were differences in early complications that were more frequent in the endoscopic group and more frequent late complications in patients undergoing surgery.
Comparison of Clinical Outcomes After Endoscopic Submucosal Dissection and Surgery in the Treatment of Early Gastric Cancer: A Single-Institute Study	The feasibility of expanding indications for submucosal endoscopic dissection to treat early gastric cancer based on long-term results showed conflicting results. This study aimed to investigate whether the results or adverse events associated with endoscopic submucosadissection are comparable to those of surgery for early gastric cancer, including absolute and expanded indications. Short-term results, clinical outcomes and adverse events were compared. Data from 159 early gastric cancers of 153 patients treated with endoscopic submucosal dissection or surgery between January 2004 and October 2014 were retrospectively reviewed. Early gastric cancers filled the absolute or expanded indications with differentiated type adenocarcinoma. Patients who met the following inclusion criteria were included in the study: (1) older than 20 years, (2) newly diagnosed with GCS without prior treatment, (3) mucosal cancer without ulcer, regardless of tumor size, (4) mucosal cancer with ulcer, ≤ 3 cm, (5) invasive cancer of the minute submucosa (submucosa 1 [SM 1], <500 μm of the muscular mucosa), ≤ 3 cm and (6) histologically differentiated adenocarcinoma. Patients with lymphovascular invasion or lymph node metastasis and those who were beyond the expanded indications for ESD were excluded. Patients who had a follow-up period of less than 1 year were also excluded. The group of endoscopic submucosal dissection and surgery showed no significant difference in the incidence of residual disease ($P = 0.48$), local recurrence ($P = 0.46$) and metachronic cancer ($P = 0.22$). Kaplan – Meier's analysis showed no significant difference in the overall survival rate at 2 years (97.6% versus [vs] 92.4%; $P = 0.45$) and 5 years (95.8% vs 95.6%; $P = 0.26$) between 2 groups. There was also no significant difference in the disease-free survival rate at 2 years (100% vs. 94.1%; $P = 0.98$) and in 5 years (100% vs 98.4%; $P = 0.89$). Early and late adverse events also showed no significant differences. For the treatment of early gastric cancer, with absolute and expanded indications, submucosal endoscopic dissection is not a lower modality in relation to clinical results and safety compared to surgery.

Propensity Score-Matched Comparison of Short-Term and Long-Term Outcomes Between Endoscopic Submucosal Dissection and Surgery for Treatment of Early Gastric Cancer in a Western Setting	Objective: This study aimed to compare the short- and long-term results of ESD and surgery for GCS. **Methods:** This retrospective case-control study included patients with CGP treated at two major cancer centers in eastern Lithuania between 2005 and 2016. All patients were Caucasian. Exclusion criteria were (1) multiple or synchronous GCS and (2) history of gastric cancer treatment, including neoadjuvant chemotherapy. Secondary endpoints included: Overall survival rate (OS) in 5 years, postoperative complication, rate, operating time and postoperative hospitalization time. The propensity score corresponding to 1: 1 of the nearest neighbor was performed, based on the clinical-pathological characteristics, among patients undergoing ESD and surgery. The primary endpoint of the study was disease-free survival (SDF) at 5 years. **Results:** Of the 260 eligible patients, 42 (16.1%) underwent SDS. After the correspondence, two well-balanced groups were analyzed, consisting of 42 patients in each. The time of operation (83 vs. 151 min., P = 0.001) and postoperative hospitalization (5.4 vs. 13.4 days, p = 0.001) were significantly lower in the group with SSD. The five-year survival rate was significantly higher in the surgery group (97.6% vs. 77.5%, p = 0.002). However, this difference was reduced after excluding cases of non-curative SDS (97.6% vs. 89.7%, p = 0.099). There was no significant difference in the 5-year SG rate between the study groups (73.8% vs. 69.0%, p = 0.599). **Conclusions:** SD canbe an excellent alternative to surgery for GPC if curative resection is achieved. Non-curative SDS is associated with poor survival and a high recurrence rate. Additional surgery should be recommended after non-curative SDS whenever the risk associated with treatment is acceptable.
Comparison of Endoscopic Resection and Gastrectomy for the Treatment of Early Gastric Cancer: A Meta-Analysis	Endoscopic resection has been one of the treatment modalities for patients with early gastric cancer. However, it has been associated with higher recurrence and metachronous cancer compared to gastrectomy. It is a meta analysis that comcants the efficacy and safety of endoscopic resection and gastrectomy for patients with early gastric cancer. "Resection en bloc" platforms "complete histological resection rates" ""duration of hospital stay" "complication rates, recurrence, metastatic cancer and survival" were sought. The inclusion criteria of the studies were: patients pathologically diagnosed with GCS; endoscopic resection was compared to gastrectomy; the quality score was greater than or equal to 5 points; studies analyzed at least 2 points (time of stay in the hospital, rate of en bloc resseccao, complete resection, recurrence of complication, metachronous cancer and survival. Reviews, case reports, guidelines articles and comments were excluded, as well as studies with patients without ECG or with tumors of other organs and without sufficient date. This meta-analysis involved 10 studies with 2070 patients: 993 patients undergoing endoscopic resection and 1077 who underwent gastrectomy. Endoscopic resection was associated with shorter hospitalization time (standardized mean difference -2.02; 95% confidence interval [CI] -2.64 to -1.39) and lower complication rate (relative risk [RR] 0.41; CI95% 0.22-0.76) than gastrectomy. However, endoscopic resection was associated with lower rates of block resection (odds ratio [OR] 0.05; CI95% 0.02-0.16) and histologically complete resection (OR 0.04; CI95% 0.01–0.11) and higher recurrence rates (RR 5.23; CI95% 2.43-11.27) and metachronic cancer (RR 5.22; CI95% 2.40-11.34) than gastrectomy. The overall survival rate (OR 1.18; CI95% 0.76-1.82) was similar. Conclusion: Endoscopic resection is minimally invasive and as effective as surgery, suggesting that the former is considered standard treatment for GCS. It should be recommended as standard treatment for GCS with indications. Additional randomized clinical trials from more countries are required.
Endoscopic Resection Versus	This article comms on the efficacy and safety of RE and GR (radical gastrectomy) for CGP in Asia. It is a meta analysis and articles published before 01/09/2017 were researched. Inclusion criteria were: all

Radical Gastrectomy for Early Gastric Cancer in Asia: A Meta-Analysis	studies comparing RE and GR for CGP; studies in Asian patients; studies that analyzed "resection en bloc", "complete resection", "complications", "recurrence", "metachronic cancer"; " 3-year survival" and "5-year survival". Exclusion criteria were: guideline articles; comments; Reviews; studies in other gastric lesions such as recurrent CGP + other gastrointestinal lesions; low-quality studies that did not have adequate data on the required characteristics, such as studies that had results < 5. Only the most informative and recent ones were chosen if they were performed by the same authors. Results: Fifteen retrospective studies were included in this analysis (3737 patients in the ER group and 4,246 patients in the RG group). No significant differences were observed in the three-year survival rate (OR, 0.87; 95% CI, 0.50-1.53) and five-year survival rate (OR, 0.81; CI 95%, 0.58-1.13) between the ER and RG groups. . Although patients submitted to RE had a higher risk of recurrence (OR, 6.07; 95% CI 4.17-8.84) and metachronic cancer occurrence (OR, 8.35; 95% CI, 5.48-12.75), recurrent or metachronic gastric cancers after RE were successfully detected and removed by endoscopic technique. Higher recurrence in the ER group may be associated with lower block resection rate (OR, 0.05; CI95%, 0.02-0.14) and complete resection rate (OR, 0.03; IC95%, 0.01-0.08). It is important to highlight that, although survival at three years and five-year survival were similar in both groups, the rate of complications in the ER group was significantly lower than in the RG group. The conclusion was that RE is a good choice for patients with small CGP lesions (less than or equal to 2cm) without lymph node metastases, especially in elderly patients with various comorbidities and in patients who cannot undergo abdominal surgery or who are within the criteria but do not accept surgery. On the other, TG is recommended when the tumor diameter is greater than 2 cm and preoperative examinations suggest the possible presence of lymph node metastasis.
Endoscopic submucosal dissection versus surgical resection for early gastric cancer: a retrospective multicenter study on immediate and long-term outcome over 5 years	This 2016 retrospective study comcants endoscopic submucosal dissection (ESD) of the stomach with surgical resection for treatment of early gastric cancer (CGP). The aim of the study was to evaluate the immediate and long-term clinical and oncological results of patients undergoing ESD, compared to those submitted to surgery. Patients from 5 centers that underwent ESD or surgery for the treatment of CGP, with expanded criteria for ESD, from 2006 to 2008 were included in this study. Results: patients submitted to ESD had shorter operating times, shorter recovery period, and shorter hospital stay when compared to patients undergoing surgical treatment. Immediate complications were more frequent in the surgical group than in the ESD group. The recurrence rate at 5 years was higher in the ESD group (12.3%) than in the surgical group (2.1%) (p = 0.001). Survival without 5-year disease was higher in the surgical group (97%) than in the ESD group (85%) (p = 0.001). Metachronic lesions were also found during the follow-up period of the ESD group. The overall 5-year survival rate was 100% for both groups. The study concludes that ESD can be an effective and acceptable treatment for CGP considering the overall survival rates with fewer complications and shorter hospital stay in relation to the surgical group. However, the article emphasizes that intensive and persistent endoscopic surveillance should be performed after ESD for early detection of metachronic lesions.
Comparison of clinical outcomes after endoscopic	In this study, data from 159 cases of early gastric cancer (CGP) of 153 patients treated with endoscopic submucosal dissection (ESD) or surgery between January 2004 and October 2014 were retrospectively

submucosal dissection and surgery in the treatment of early gastric cancer	reviewed. The cases in question filled out the absolute or expanded indications with adenocarcinoma of the differentiated type. The inclusion criteria for this study were: a) Patients older than 20 years b) Patients recently diagnosed with CGP, without prior treatment c) Mucous cancer without ulcers, regardless of tumor size d) Mucous cancer with ulcer ≤ 3cm e) minute (submucosal 1 [SM 1], <500 μm from the muscularis mucosa) submucosal invasive cancer, ≤3 cm f) Differentiated type adenocarcinoma Exclusion criteria for this study were: a) Patients with lymphovascular invasion or lymph node metastasis and those who did not meet the expanded criteria for indication of ESD b) Patients with less than 1 year of follow-up Seventy-four patients underwent ESD, and 79 underwent surgery. The mean follow-up time in the ESD group was 2 years, while in the surgical group it was 3 years. Tumors in the ESD group were significantly smaller than in the surgical group (9mm and 15mm, respectively); $p < 0.001$), and most of them were located in the lower third of the stomach. Abbreviations: OS = overall survival; DFS = disease-free survival Results: The 2-year OS rate was 97.6% in the ESD group and 92.4% in the surgical group. The 5-year OS rate was 95.8% in the ESD group and 95.6% in the surgical group. The DFS rate of 2 and 5 years was 100% in the ESD group. In the surgical group, the DFS rate of 2 years and 5 years were 94.1% and 98.4%, respectively. Early adverse events occurred in 9 patients (12.2%) in the ESD group, and in 5 patients (6.3%) in the surgical group. The most common adverse event in the ESD group was bleeding, and the 2nd most common was gastric perforation. Late complications occurred only in the surgical group. The study concludes that long-term clinical outcomes such as local recurrence, metachronic cancer, OS rate, DFS, and late adverse events after ESD were comparable to the surgical group for cgp treatment. The authors point out that the study had many limitations. As this is a retrospective study, there may be bias. As an example, it is cited that the ESD group may have its results positively biased due to minor and non-malignant lesions that were observed via histology in the pre-treatment period. In addition, the follow-up period was different in the ESD group compared to the surgical group, and it is possible that the mean follow-up duration was not sufficient to evaluate the long-term results. According to the authors, the main cause of loss of follow-up is probably the vast possibility of endoscopic evaluation in local clinics. The study concludes that due to the increasing screening of cancer, and the advantages of endoscopic treatment, the proportion of CGP treated with ESD is expected to increase. Furthermore, it is emphasized that ESD may be a comparable choice, instead of surgery, to treat GC that meet the absolute and expanded indications.
Long-term Survival After	The aim of the study was to evaluate the long-term results of endoscopic resection compared to surgery for early gastric cancer that met the expanded indication.

Endoscopic Resection Versus Surgery in Early Gastric Cancers	Data from patients undergoing endoscopic resection or surgery for gastric cancer that met the expanded indication between 2001 and 2009 were retrospectively analyzed. The overall survival rate was the primary outcome; recurrence rates of gastric cancer and complications were secondary outcomes. Among the 457 patients included, 165 underwent endoscopic resection and 292 surgeries, with a mean follow-up time of 58.6 months. Overall 5-year survival rates were 97.5% and 97.0% for endoscopic resection and surgery, respectively; there was no significant difference (P = 0.425). The recurrence rate of trictric cancer at 5 years was higher in endoscopic resection than in surgery (4.8% vs. 0.3%; P <0.001) mainly because of metachronic cancers that developed only in the endoscopic resection group (9/165, 5.5%). Most metachronic cancers (88.9%) were treated curly with endoscopic resection. The rates of early complications were similar between the groups (P = 0.557), but the endoscopic resection group had more complications of grade III or higher, according to the Classification of Clavien – Dindo, compared to the surgical group (4.8% vs. 1.4%, P = 0.026) . Late complications occurred only after surgery (4.8%, P = 0.004), and the majority (92.9%) were grade III or higher. Conclusions: Endoscopic resection may be an ideal alternative to gastric cancer surgery that meets expanded indication criteria due to a comparable overall long-term survival rate.
Comparing Laparoscopic to Endoscopic Resections for Early Gastric Cancer in a High Volume North American Center	It is a study from North America that performs the comparison between endoscopic submucosal dissection and laparoscopic gastrectomy, evaluating the results of these procedures when performed in malignant and premalignant gastric tumors in early gastric cancer. The study was based on a total of 155 patients who underwent any of these treatments for adenocarcinoma or dysplasia at the McGrill University Health Center. The study was conducted retrospectively at a teaching hospital in North America, evaluating the medical records of all patients who underwent endoscopic or laparoscopic treatment for adenocarcinoma or gastric adenomatous polyps with dysplasia, from February 2007 to March 2014. Squamous or neuroendocrine cell tumors were excluded. The following were analyzed: demography of the patient, tumor characteristics, oncological results, permanence, postoperative complications and follow-up data after treatment. The cases were dichotomized according to resection method, including the endoscopic method (from 2009), and all procedures were performed by the same surgeon. Of the 115 patients, 37 were treated with laparoscopy and 30 patients were submitted to the endoscopic method, while the rest were discarded by exclusion criteria. The results showed that even though there was no significant difference in the rate of postoperative complications between the two groups, the severity of complications was higher in patients undergoing laparoscopic resection. In terms of survival, data were collected from only 61 patients, which showed that there is no significant difference between the two groups in terms of disease-free follow-up. Overall survival was 100% at 4 years in the group that underwent endoscopic dissection, and 90.3% in the laparoscopic resection group. Disease-free survival was 84.6% in 4 years in the endoscopic method group, and 82.6% in the laparoscopic group. However, given the heterogeneity of tumors in both groups, the analysis was performed again in patients with T1 lesions only, resulting in disease-free survival rates of 100% in the group submitted to laparoscopy and 88.9% in the group submitted to endoscopy. The study concluded that the endoscopic method is safe for selected cases of early gastric cancer, since morbidity was lower than in the laparoscopic method. However, a longer follow-up study is necessary to complement the results of this study, since, at the time of publication of this study, there were no other similar studies published.

Comparison of endoscopic submucosal dissection with surgical gastrectomy for early gastric cancer: An updated meta-analysis.	It is a study published in 2019, which used the prism method to compare the safety and efficacy in the short and long term between the results of endoscopic vs. surgical treatment. The database used for the research were: pubmed, embase, web of science and cochrane library from January 1990 to June 2018, encompassing studies with short to long-term results for comparison. Inclusion criteria were: studies involving patients diagnosed with early gastric cancer based on histology, studies conducted to compare the two types of treatment, studies reporting clinical results after the endoscopic or surgical procedure, including results of long-term survival or event-free survival. Exclusion criteria were: case reports or reviews, treatment performed in other pathological types of gastric cancer other than adenocarcinoma, involvement of hybrid treatment techniques, studies including less than 20 patients in each group. We included 14 articles to perform this work. The results of the meta-analysis demonstrated some advantages of the endoscopic procedure, such as decreased operative time, shorter hospital stay and lower rates of postoperative complications. However, patients undergoing endoscopic treatment have higher recurrence rates than patients undergoing surgery. This meta-analysis also has several limitations that must be addressed. First, the clinical heterogeneity of the included studies. Second, the retrospective nature of the studies submitted limited the application of the results. Third, only one Western study of Canada has been entered and the conclusion may not apply in Western countries. In conclusion, this meta-analysis suggested that endoscopy is safe and feasible compared to resection surgery in the treatment of early gastric cancer, with clinical advantages in time of operation, hospitalization, postoperative complications. Although some differences in tumor recurrence rate, long-term survival also supported the safety of endoscopy compared to resection surgery.
Long-Term Outcomes Comparison of Endoscopic Resection With Gastrectomy for Treatment of Early Gastric Cancer: A Systematic Review and Meta-Analysis.	Comparison of long-term results of endoscopic resection with gastrectomy for early gastric cancer treatment: a systematic review and meta-analysis. Results: Nine studies were included in this systematic review; treatment with RE was associated with a shorter length of stay (ROM = -8.53, 95%CI -11.56 to -5.49), fewer postoperative complications (OR = 0.47, 95%CI 0.34- 0.65). ER can be performed safely, with less hospital stay and fewer postoperative complications than gastrectomy. The recurrence rate was higher in RE than in the treatment of gastrectomy (HR = 3.56, 95% CI 1.86–6.84), mainly because metachronic gastric cancers developed only in the treatment of RE. However, most metachronic gastric cancers can be curatively treated with ER again, and this does not affect the overall survival of patients with early gastric cancer. There was no difference in the overall survival rate between RE and gastrectomy (HR = 0.84, 95% CI 0.63-1.13). Conclusions: ER and gastrectomy are acceptable for the curative treatment of early gastric cancer. However, due to comparable overall survival and lower postoperative complications and shorter hospital stay, RE is better than gastrectomy for early gastric cancer, which met the indication for TREATMENT WITH RE. Methods Research strategy: We conducted and reported this systematic review and meta-analysis following the PRISMA statement. The research words are "early gastric cancer", "early stomach cancer", "early stomach neoplasia", "ESD", "EMR", "endoscopic resection" and "gastrectomy". A search was conducted in the Pubmed, Embase and Cochrane Library databases. Studies comparing ER with gastrectomy for early gastric cancer were included in this meta-analysis. We researched

clinical studies published before March 2019. Meanwhile, we try to find relevant literature through references from clinical studies. We then read the full text and determine the eligible studies. Finally, a total of nine studies were included in the analysis.

Include and exclude patterns

The studies were acceptable in a systematic review if they met these standards: The research compared the results of ER and gastrectomy; The research reported at least one of the following clinical outcomes, including hospital stay, postoperative complications, disease-free survival, and overall survival; The research was published as a full text in the English language. Search that failed to extract effective data or provide the full text was deleted.

The inclusion criteria of the patients: newly diagnosed as early gastric cancer, histologically confirmed adenocarcinoma limited to the mucosa or submucosa (stage TNM 0-IIIB) and received gastrectomy or ER for treatment. The exclusion criteria of patients: submitted to previous gastrectomy. Postoperative pathological evaluation was performed in all studies included. A clear surgical margin was confirmed by pathological evaluation. If a clear surgical margin was not reached in the patients, these patients required additional ER or gastrectomy. And, patients requiring additional gastrectomy were excluded from the study.

Length of hospital stay: five studies reported data on length of stay. Due to the significant heterogeneity (I2 = 91.2%, P = 0.000), a random effect model was used. There was a significant difference in the length of stay between THE and gastrectomy treatment for early gastric cancer. Treatment with RE was associated with a shorter hospital stay than treatment with gastrectomy (ROM = -8.53, 95% CI -11.56 to -5.49). In the expanded indication subgroup, the difference in length of stay between ER and gastrectomy was also statistically significant (ROM = -6.2, 95%CI -9.45 to -2.94; Figure 3). In the ESD subgroup, there was also a significant difference in the length of stay (ROM = -5.63, 95% CI -7.05 to -4.21).

Postoperative complications: All nine studies included postoperative complications. There was no significant heterogeneity (I2 = 46.9%, P = 0.058), and a fixed effect model was used. The incidence of postoperative complications of gastrectomy treatment was higher than that of TREATMENT with RE (OR = 0.47, 95% CI 0.34-0.65). In the expanded indication subgroup and ESD, there was also a significant difference in complications.

Disease-free survival: In this meta-analysis, five studies included disease-free survival. Because of no significant heterogeneity (I2 = 45.1%, P = 0.122), a fixed effect model was used. Patients undergoing TREATMENT with RE had a higher recurrence rate than gastrectomy (HR = 3.56, 95% CI 1.86-6.84). The results showed that the recurrence rate of ER treatment was significantly higher than that of gastrectomy treatment. This was probably due to the residual gastric mucosa, which may contain areas at high risk of developing metachronic gastric cancer. Additional treatments for recurrent lesions should be considered in patients with early gastric cancer after RE, but current studies have not shown any adverse events after additional endoscopic treatments for metachronic lesions, and overall early gastric cancer survival showed no significant difference between ER and gastrectomy. In the expanded indication subgroup and ESD, there was also a significant difference in disease-free survival between ER and gastrectomy.

Overall survival: overall survival data have been reported in eight studies. Because there was no significant heterogeneity (I2 = 26.5%, P = 0.217), a fixed-effect model was used. Overall survival

did not differ between RE and gastrectomy treatment (HR = 0.84, 95% CI 0.63-1.13). In the analysis of subgroups, there was also no significant difference in overall survival.

Discussion

In recent years, with the development of digestive endoscopic techniques, more and more early gastric cancer has been found in the absence of symptoms. The treatment of gastrectomy was performed as a conventional treatment for early gastric cancer. However, in selected early gastric cancer, THE is accepted due to its minimal invasion and better quality of life after the procedure. In recent years, ER has become the minimum treatment for early gastric cancer.

According to Japanese guidelines for the treatment of gastric cancer, ER includes EMR and ESD. And ER is indicated as standard treatment for the following tumor: a differentiated type adenocarcinoma without UL ulcerative findings (-), whose depth of invasion is clinically diagnosed as T1a and the diameter is ≤2 cm. The expanded indication is that tumors clinically diagnosed as T1a and: (a) of differentiated type, UL (-), but with more than 2 cm in diameter. (b) of differentiated type, UL (+) and ≤ 3 cm in diameter. (c) of undifferentiated type, UL (-) and ≤2 cm in diameter.

The ER was a minimally invasive treatment for early gastric cancer, which met the guidelines or expanded criteria (32). However, the clinical results of ER remain controversial, several recent reports suggest that lymph node metastases may occur after treatment of ER in early gastric cancer. Therefore, the results of ER treatment are still controversial for early gastric cancer. This meta-analysis combined the results of several individual studies to evaluate the results of THE.

In this meta-analysis, a total of nine studies analyzing the treatment of endoscopy resection and gastrectomy were included. This meta-analysis showed that the treatment with RE showed some advantages, had a significantly shorter length of stay and lower rates of postoperative complications. And there was no significant difference between ER and gastrectomy treatments in the overall survival of early gastric cancer. These results of length of stay, postoperative complications and overall survival were consistent with those of other meta-analyses.

There was much evidence to show that the recurrence rate of ER treatment was significantly higher than that of gastrectomy treatment, and recurrence rates with RE were 4.7 to 11.1%, and gastrectomy recurrence rates were from 0.0 to 1.1%. In these results, the risk of tumor recurrence was significantly higher in the ER group than in the surgical group. This was probably due to the residual gastric mucosa, which may contain areas at high risk of developing metachronic gastric cancer, such as mucosa with atrophic gastritis and intestinal metaplasia. Additional treatments for recurrent lesions should be considered in patients with early gastric cancer after RE, but current studies have not shown any adverse events after additional endoscopic treatments for metachronic lesions, and overall early gastric cancer survival showed no significant difference between ER and gastrectomy treatment. And, metachronic gastric cancer did not affect overall survival.

In conclusion, ER and gastrectomy are both acceptable for curative treatments of early gastric cancer. However, ER is better than gastrectomy for early gastric cancer, which was indicated for ER treatment due to comparable overall survival and lower postoperative complications and shorter hospital stay.

Endoscopy vs Surgery in the Treatment of Early Gastric Cancer: Systematic Review	This systematic review involves 2,654 patients who met absolute or expanded criteria for endoscopic resection. This research was developed to establish the short- and long-term outcomes of endoscopic resection compared to surgery in the treatment of CGP, better supporting clinical practice. The systematic review with meta-analyses was carried out using the Medline, Embase, Cochrane, LILACS, Scopus and CINAHL databases. In total, 11 retrospective cohorts were used for quantitative and qualitative analysis. Among the different modalities of endoscopic treatment, resection procedures were the most used for evaluation, such as *mucosal endoscopic resection (EMR) and submucosal endoscopic dissection (ESD).* In this study, only gastric adenocarcinoma was considered. No other types of neoplasms such as lymphomas or stromal tumors were considered, for example. The eligibility criteria for the review were: a) Types of studies: clinical trials and/or observational studies of appropriate methodological quality were selected for inclusion in this review b) Types of patients: patients diagnosed with CGP c) Types of interventions: Comparative studies of treatment outcomes in two modalities: surgical and endoscopic treatment d) Types of outcomes evaluated: the outcomes evaluated were survival rate in three, five and ten years, complications, complete resection, recurrence and mortality. Findings 3-year survival data were available in six studies (n = 1197). There was no difference in risk (DR) after the 2 treatments (DR = 0.01, confidence interval (CI) 95% = -0.02 to 0.05). There was no significant difference in 5-year survival between the groups analyzed (DR = 0.01, CI 95% = -0.01 to 0.03). In the evaluation of 551 patients, there was no inequality in 10-year survival between the different approaches (DR = -0.02, 95% CI = -0.15 to 0.10). Of the 11 studies in question, only 8 (n = 2439) included data on complications. In this ite, there was a significant difference (DR = -0.08, CI 95% = -0.10 to -0.05), demonstrating better results with the endoscopic approach. Complete resection rates were studied in 536 patients. Again, there was a significant difference (DR = -0.13, 95% CI = -0.17 to -0.09), giving better results to patients undergoing the surgical approach. The recurrence rate was evaluated in five studies (n = 1331) and there was no difference between the two approaches (DR = 0.01, 95% CI = -0.00 to 0.02). Mortality rates were studied in four studies (n = 1107), and there was no difference between the groups studied (DR = -0.01, 95% CI = -0.02 to 0.00). The systematic review concludes that: - survival rates of 3, 5 and 10 years are similar for patients undergoing endoscopic or surgical treatment, as well as mortality and recurrence rates. - complication rates are lower in patients undergoing endoscopic treatment - complete resection rates are higher in patients undergoing surgical treatment - if there is adequate infrastructure, the endoscopic approach should be taken as an initial treatment for patients with GPC
Updated Evaluation of Endoscopic	This publication involves 5993 patients, through 18 retrospective studies. Of these 5,993 patients, 2,694 underwent endoscopic submucosal dissection, and the other 3,299 underwent surgery. This article was

Submucosal Dissection Versus Surgery for Early Gastric Cancer: A Systematic Review and Meta-Analysis	made using the PubMed, Web of Science, EMBASE, Cochrane Library Databases and Google Scholar databases. Only studies published in English were considered for this research. The inclusion criteria for the review were: a) Types of patients: people diagnosed with early gastric cancer (GPC), through pathological evidence b) Types of interventions: use of *submucosal endoscopic dissection (ESD)* in selected patients. Comparing them with patients submitted to type D1 or D2 lymphadenectomy, either openly or laparoscopically c) Types of measure of results: report at least one of the parameters listed (hospital cost, operating time, histologically complete resection, curative resection, recurrence, survival, among others) d) Types of studies: randomized clinical trials, prospective or retrospective cohort, and case-control studies The exclusion criteria for the review were: (a) types of studies: studies which were only reviews or abstracts; animal studies b) Studies including benign diseases such as polyps (c) studies covering non-gastric or hybrid lesions d) Studies that did not include the results measures that were outlined by the authors of this review (e) studies dealing with interventions other than ESD, or which only referred to endoscopic resection, without clearly illustrating it f) In scores less than 5 points The study concludes that: The ESD procedure has a marked advantage over surgical treatment, in terms of shorter operating time. Deaths related to the procedure only occurred in the group submitted to surgery. The total number of adverse events was lower in the group submitted to ESD, as well as shorter hospital stay, less trauma, and better quality of life. In addition, the ESD proved to be a cheaper procedure. The most common complications in patients undergoing ESD are perforation and bleeding. However, in most cases, these complications can be resolved through endoscopic treatment. As reported in other meta-analyses, the study concludes that the risk of recurrence is higher in the ESD group. In summary, the conclusion is that ESD is a cheaper method, with lower operative morbidity, less traumatic, of faster recovery and that confers better quality of life to the patient. However, ESD is related to a higher risk of recurrence.

9.2 OUTCOME ON THE OVERALL SURVIVAL RATE:

Of the 19 articles selected, all evaluated the overall survival rate. Eight of these studies (Kaiyu Sun et al,2015, Fan-Sheng Meng et al, 2015, Lihu Gu et al, 2019, Joo Hyun Lim et al, 2019, Young-Il Kim et al, 2015, Sara Najmeh et al, 2016, Hua Li et al, 2016, Liangliang An et al, 2019) showed no significant differences in overall survival of endoscopic resection with gastrectomy. One study (Ji Young Chang et al, 2017) showed no significant differences in overall survival of endoscopic resection with gastrectomy at 2

years. Three of these studies (Fei-Long Ning et al, 2017, Weili Sunet al, 2015, 19 Qing Liu et al 2019) showed no significant differences in the overall survival of endoscopic resection with gastrectomy at 3 years. Eight of these studies (Fei-Long Ning et al, 2017, Weili Sunet al, 2015, 19 Qing Liu et al 2019, Ji Young Chang et al, 2017, Shuanhu Wang et al, 2015, R Bausys et al 2019, Seung Jee Ryu et al, 2016, André Kondo et al, 2015) showed no significant differences in overall survival of endoscopic resection with gastrectomy at 5 years. Three of these studies (Jeung Hui Pyo et al, 2016, Weili Sunet al, 2015, 19 Qing Liu et al 2019) showed no significant differences in the overall survival of endoscopic resection with gastrectomy in 10 years. One study (MirMilad Khoshknab et al, 2020) showed that the survival rate was higher in patients treated with gastrectomy than with endoscopic resection. Finally, a study (Junbi Hu et al, 2018) showed that the 3-year survival rate in the surgery group was significantly higher than in the ESD group.

9.3 OUTCOME ON THE RISK RATE:

Of the 19 articles, two assessed the risk of perforation during the procedure. An article concludes that the perforation during the procedure in the ESD group was higher than in the surgical group. Another cites gastric perforation during the procedure as the second most common adverse event in the ESD group.

9.4 OUTCOME ON THE ADVERSE EVENT RATE:

Of the 19 articles selected, fourteen evaluated the rate of adverse events/complications. Of these fourteen, nine articles (64.3%) [Junbi Hu et al, 2018; Fan-Sheng Meng et al, 2015; Weili Sun et al, 2015; Shuanhu Wang et al, 2015; Fei-Long Ning et al, 2017; Hua Li et al, 2019; Liangliang An et al, 2019; André Kondo et al, 2015; Qing Liu et al, 2019] conclude that the ESD group had a lower rate of adverse events or complications. Two articles (14.28%) [Ji Young Chan et al, 2017; Sara Najmeh et al, 2016] conclude that there is no significant difference in the rate of adverse events/complications between the two treatment modalities. An article (7.14%) [Seung Jee Ryu et al, 2016] concludes that immediate complications are more frequent in the gastrectomy group. An article (7.14%) [Jeung Hui Pyo et al, 2016] concludes that the ESD group had more immediate complications, while the group submitted to gastrectomy presented more late complications**.** An article (7.14%) [Young-Il Kim et al, 2015] concludes that immediate complications are similar in both groups, while late complications only occurred in the group submitted to gastrectomy.

9.5 OUTCOME ON RECURRENCE RATE:

Of the 19 articles selected, only 16 presented results regarding gastric cancer recurrence rates comparing endoscopic and surgical resection methods. Of these sixteen, two articles [Ji Young Chang et al., 2017; André Kondo et al., 2015] reported not finding significant differences between the rates of the two therapeutic methods. Quatroze articles [Kaiyu Sun et al., 2015; Junbi Hu et al., 2016; Fan-Sheng Meng et al., 2015; Weili Sun et al., 2015; Lihu Gu et al., 2019; Lim JH et al., 2019; Jeung Hui Pyo et al.,

2016; R Bausys et al., 2019; Fei-Long Ning et al., 2017; Seung Jee Ryu et al., 2016; Young-II Kim et al., 2015; Hua Li et al., 2019; Liangliang An et al., 2019; Qing Liu et al., 2019] obtained concrete data to conclude that recurrence rates were significantly higher in the group that underwent endoscopic resection when compared to the group submitted to gastrectomy. Among the 3 remaining articles, two articles [Shuanhu Wang et al., 2015; MirMilad Khoshknab Pourmousavi et al., 2020] did not analyze recurrence and an article [Sara Najmeh et al., 2016] did not obtain enough data for completion.

9.5.1 Outcome on hospital stay:

Of the 19 articles selected, fourteen of them compared the time of hospitalization between patients who underwent gastrectomy and patients who underwent endoscopic resection. Of these fourteen, all [Kaiyu Sun et al., 2015; Junbi Hu et al., 2016; Fan-Sheng Meng et al., 2015; Weili Sun et al., 2015; Shuanhu Wang et al., 2015; MirMilad Khoshknab Pourmousavi et al., 2020; Jeung Hui Pyo et al., 2016; R Bausys et al., 2019; Seung Jee Ryu et al., 2016; Sara Najmeh et al., 2016; Hua Li et al., 2019; Liangliang An et al., 2019; André Kondo et al., 2015; Qing Liu et al., 2019] concluded that patients undergoing endoscopic resection have shorter hospital stay. Among the 5 remaining articles [Lihu Gu et al., 2019; Lim JH et al., 2019; Ji Young Chang et al., 2017; Fei-Long Ning et al., 2017; Young-II Kim et al., 2015], all five did not comment on the time of hospitalization.

9.5.2 Outcome about age:

Of the 19 articles selected, eight [Kaiyu Sun et al, 2015; Junbi Hu et al, 2018; Shuanhu Wang et al, 2015; Ji Young Chan et al, 2017; Fei-Long Ning et al, 2017; Hua Li et al, 2019; Liangliang Na et al, 2019; Qing Liu et al, 2019] took into account the average age of patients. Of these eight, the mean age in the ESD group was 65.5 years, while the surgical group was 63.7 years. The lowest mean age in the ESD group was 63.7 years [Qing Liu et al, 2019], while the highest was 67 years [Shuanhu Wang et al, 2015]. The lowest mean age in the surgical group was 61.4 years [Qing Liu et al, 2019], while the highest was 67.15 years [Liangliang Na et al, 2019].

9.5.3 Outcome about sex:

Of the 19 selected studies, eleven mention the prevalence of genders. Of these eleven, ten articles [Kaiyu Sun et al, 2015; Junbi Hu et al, 2018; Jeung Hui Pyo et al, 2016; Ji Young Chang et al, 2017; R Bausys et al, 2019; Seung Jee Ryu et al, 2016; Young-Il Kim et al, 2015; Sara Najmeh et al, 2016; Hua Li et al, 2019; Liangliang An et al, 2019] show that most of the patients analyzed were male and only one article [Joo Hyun Lim et al 2019] shows that most of the patients analyzed were female.

9.5.4 Outcome on h. pylori's research:

When the presence of Helicobacter pylori was researched in these patients, we did not find data in relation to this. However, of the 19 articles selected, six of them addressed helicobacter pylori. Of these six: three articles Weili Sun et al., 2015; Lihu Gu et al., 2019; Young-II Kim et al., 2015] showed that the eradication of Helicobacter pylori in patients who underwent endoscopic resection for early gastric cancer could reduce the occurrence of metachronic gastric cancer; an article [Sara Najmeh et al., 2016] commented that overall incidence rates of gastric cancer have decreased and this has been attributed to dweller changes and reduced rates of chronic Helicobacter pylori infection; and an article [Qing Liu et al., 2019] reported that the vast majority of gastric cancer cases are related to inadequate standards of hygiene and H infection. Pylori. In addition, it suggested that the successful eradication of H. pylori may be effective for the prevention of metachronic cancer after curative endoscopic resection of early gastric cancer. Of the remaining 13 [Kaiyu Sun et al., 2015; Junbi Hu et al., 2016; Fan-Sheng Meng et al., 2015; Shuanhu Wang et al., 2015; Lim JH et al., 2019; MirMilad Khoshknab Pourmousavi et al., 2020; Ji Young Chang et al., 2017; R Bausys et al., 2019; Fei-Long Ning et al., 2017; Seung Jee Ryu et al., 2016; Hua Li et al., 2019; Liangliang An et al., 2019; André Kondo et al., 2015] all thirteen did not comment on H's research. Pylori.

9.5.5 Outcome on ethnicity:

In addition, 17 articles referred to the countries of origin of the studies. The results found were, in this order: South Korea (in 14 papers), Japan (10) and China (9), Canada (5), Hong Kong (2) and Lithuania (1).

9.5.6 Outcome on cost:

Only 3 articles analyzed the costs of endoscopic resecccao and gastrectomy, which were: Junbi Hu et al, 2018; Fan-Sheng Meng et al, 2016; Weili Sun et al, 2015. All 3 concluded that endoscopic resection is less costly than gastrectomy.

10 DISCUSSION

Regarding overall survival, the 19 studies evaluated this outcome. In 17 of them there were no differences between gastrectomy and endoscopic resection, either in 2, 3, 5 and 10 years. Only 2 studies showed that survival rates were higher at gastrectomy. Among the results of the old days there was a prevalence of better survival outcomes in gastrectomy, but this indifference in the results obtained is probably due to advances in endoscopic techniques that provide lower rates of error in the procedure and a greater precision in tumor removal.

Regarding the adverse event rate, 14 studies evaluated this variable. Nine of them conclude that the ESD group had a lower rate of adverse events or complications; two articles conclude that there is no significant difference in the rate of adverse events or complications between the two treatment modalities; and one article concludes that immediate complications are more frequent in the gastrectomy group. In addition, an article concludes that the ESD group had more immediate complications, while the group submitted to gastrectomy presented more late complications**.** In addition, another article concludes that the immediate complications are similar in both groups, while late complications only occurred in the group submitted to gastrectomy. Therefore, there was a prevalence in the results of lower adverse effect rates in ESD and this is probably due to the higher risk of infection that open surgery brings. Moreover, the endoscopic technique is less invasive and maintains the anatomical integrity of the stomach.

Regarding the risk rate, only two articles assessed the risk of perforation during the procedure. One of them concludes that perforation during the procedure in the ESD group was higher than in the surgical group; while the other cites gastric perforation during the procedure as the second most common adverse event in the ESD group. Although the result is inconclusive, it is widely discussed that the risk of perforation is higher in endoscopy because it is a procedure with a smaller field of surgical view. However, with advances in endoscopic technique, this risk tends to decrease as time goes by.

Regarding the recurrence rate of gastric cancer between the two techniques, 16 studies showed results. Among them, two articles reported not finding significant differences between the rates of the two therapeutic methods and fourteen articles obtained concrete data to conclude that recurrence rates were significantly higher in the group that underwent endoscopic resection when compared to the group submitted to gastrectomy. This is probably justified by the non-total resection of the tumor by endoscopic technique compared to gastrectomy, due to the lower visual field during the procedures and lower mobility of the surgeon.

Regarding the time of hospitalization, 14 of them compared this outcome. Of these, all concluded that patients submitted to endoscopic resection had shorter hospital stay. One hypothesis for this fact would be the smaller incision in the patient and because it is a smaller surgery, having fewer adverse events with lower risk of infection, which provides a faster recovery.

Regarding cost, 3 articles analyzed this variable and all concluded that endoscopic resection is less costly than surgery. This is due to the fact that, because it is a smaller surgery it requires fewer materials, anesthesia, auxiliary professionals, requires a shorter hospital stay and has fewer adverse effects.

Epidemiological Profile of the Sample:

Regarding age, eight took into account the mean age of the patients. Of these 8, the mean age in the ESD group was 65.5 years, while the surgical group was 63.7 years. The mean age was similar in both techniques and older age was found because it is a multifactorial chronic disease that, although it has genetic factors involved, greater environmental exposure increases the risks of developing this disease. We

expected to find a higher rate of older patients in endoscopic techniques, since being less invasive brings fewer risks, but was not found.

Regarding gender, 11 studies mention the prevalence of genders. Ten of them show that most of the patients analyzed were male and an article shows that most of the patients analyzed were female. The epidemiology found actually shows a higher prevalence in men and this is probably due to the habits of higher alcohol consumption, higher smoking, sedentary lifestyle and lower demand for physicians.

Regarding ethnicity, most patients were from Asian countries and this is justified by the fact that the studies used in this horizontal review are studies done in such countries.

In relation to H's research. pylori, we found no data in your relationship. It was researched in order to analyze a possible relationship between H. positive pylori in the patient and increased chances of developing a gastric cancer and whether there would be any comparison between the two techniques. However, no such comparison was observed in our studies. However, six studies mention *H. Pylori*. Of these six, three articles showed that the eradication of Helicobacter pylori in patients who underwent endoscopic resection for early gastric cancer could reduce the occurrence of metachronic gastric cancer. An article commented that overall incidence rates of gastric cancer have decreased and this has been attributed to dweller changes and reduced rates of chronic Helicobacter pylori infection. One article reported that the vast majority of gastric cancer cases are related to inadequate standards of hygiene and H *infection. Pylori*. In addition, it has been suggested that successful *eradication of Helicobacter pylori* may be effective for the prevention of metachronic cancer after curative endoscopic resection of early gastric cancer.

11 CONCLUSION

Regarding survival, there was no statistical difference in the results obtained. This is probably due to advances in endoscopic techniques that provide lower rates of error in the procedure and greater precision in tumor removal.

Regarding the rate of adverse events, the lowest rates of adverse effect in ESD are probably justified by the higher risk of infection that open surgery brings and the endoscopic technique being less invasive and maintaining the anatomical integrity of the stomach.

Regarding the risk rate, despite the inconclusive result, in fact the endoscopic technique tends to have a higher risk for having a smaller field of view, but we conclude that with the advances in this technique this risk tends to decrease as time passes.

Regarding the recurrence rate, they were significantly higher in the group that underwent endoscopic resection and this is probably justified by the non-total resection of the tumor by endoscopic technique compared to gastrectomy, due to the lower visual field during the procedures and lower mobility of the surgeon.

Regarding the time of hospitalization, patients submitted to endoscopic resection technique were hospitalized for less time and a hypothesis for this fact would be the smaller incision in the patient and because it is a smaller surgery, having fewer adverse events with lower risk of infection, which provides a faster recovery.

In relation to cost, endoscopic resection is in fact less costly than surgery and this is due to the fact that, because it is a smaller surgery it requires fewer materials, anesthesia, auxiliary professionals, requires a shorter hospital stay and has fewer adverse effects.

Regarding age , the mean was similar in both techniques and older age was found because it is a multifactorial chronic disease that, although it has genetic factors involved, greater environmental exposure increases the risks of developing this disease. We expected to find a higher rate of older patients in endoscopic techniques, since being less invasive brings fewer risks, but was not found.

In relation to gender, the epidemiology found actually showed a higher prevalence in men and this is probably due to habits of higher alcohol consumption, higher smoking, sedentary lifestyle and lower demand for physicians.

Regarding ethnicity, most patients were from Asian countries and this is justified by the fact that the studies used in this horizontal review are studies done in such countries.

Regarding H pylori's research we wanted to analyze a possible relationship between H. positive pylori in the patient and increased chances of developing a gastric cancer and whether there would be any comparison between the two techniques. However, no such comparison was observed in our studies.

From the above, it is possible to conclude with property that the technique of RE in early adenocarcinoma stage 0 is more advantageous than gastrectomy in several aspects.

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