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Do we adequately diagnose early gastric cancer in Turkey

Hüsnü Oğuz KOÇ, Yavuz Selim SARI, Hasan BEKTAŞ, Vahit TUNALI, Orhan ŞAHİN, Kerim ÖZAKAY, Ersöz FEYZULLAH

Department of General Surgery, Ministry of Health, İstanbul Education and Research Hospital, İstanbul

Background/aims: *Late diagnosis of patients with advanced gastric cancer is due to late admission of patients or overlooked early gastric cancers in early endoscopies. We retrospectively evaluated gastroscopic results in our clinic over 9 years and assessed outcomes of all patients diagnosed and treated for gastric cancers, including early gastric cancers.* ***Materials and Methods:*** *We retrospectively evaluated all gastroscopic reports in our hospital between January 2000 and January 2009, dividing these patients into two time periods: 2000–2004 and 2005–2009. For all patients with early gastric cancers, we assessed age, gender, macroscopic tumor type, location in the stomach, type of surgery, histopathological verification of the tumor, lymph node involvement and general patient condition.* ***Results:*** *Of the 37,768 patients who underwent gastroscopy, 3.53% (536 patients) during 2000–2004 and 4.3% (973 patients) during 2005–2009 were diagnosed with gastric cancer. During these two time periods, 21 (3.91%) and 61 (6.26%), respectively, of the patients who underwent radical surgical intervention were diagnosed with histopathologically proven early gastric cancers.* ***Conclusion:*** *The rate of early gastric cancers among patients with gastric cancer was lower in Turkey than in western countries and Japan. As in other western countries, screening endoscopy is not feasible in Turkey. The use of chromoendoscopy and magnified endoscopy, particularly in patients with alarm symptoms and in risk groups, may increase the rate of early diagnosis.*

Key words: Early gastric cancer, chromoendoscopy, endoscopic submucosal dissection

Türkiye'de erken mide kanseri tanısında yeterli miyiz?

Amaç: *İleri evre mide kanseri, genellikle erken evre mide kanserli olguların endoskopide gözden kaçması veya hastaların geç gelmesi nedeni ile olmaktadır. Hastanemizde 9 yıl süresince endoskopik olarak tanısı konulmuş ve cerrahi tedavileri yapılmış erken veya geç yakalanmış mide kanserli olguları retrospektif olarak değerlendirmek istedik.* ***Metod:*** *Ocak-2000 tarihinden başlayarak Ocak-2009 tarihine kadar hastanemizde yapılan tüm gastroskopilerin raporlarına digital arşivden ulaşıldı. Çalışmada olgular 2000-2005 ve 2005-2009 tarihleri olarak iki bölüme ayrılarak incelendi. Bu dosyalardaki veriler doğrultusunda hastanemizde yapılan toplam gastroskopi sayısı, toplam endoskopik mide kanseri tanısı, patolojik tanısı mide kanseri olan toplam hasta sayısı, toplam erken ve ileri evre mide kanserleri sayısı, toplam inoperabl mide kanseri sayısı, toplam laparotomi sayısı, erken mide kanseri tanısı alan hastaların yaşı, cinsiyeti, tümörün makroskopik tipi, tümörün histolojik tipi, lenf nodu tutulumu, midede yerleşim yeri, yapılan ameliyat, hastaların yaşam durumları incelendi ve kaydedildi.* ***Bulgular:*** *2000-2005 yıllarında yapılan toplam 15.174 gastroskopik incelemede, 536 (%3.53) hastaya, 2005-2009 yıllarında yapılan 22.594 gastroskopik incelemede de toplam 973 (%4.30) hastaya mide kanseri tanısı konulmuştur. Toplamda 1509 hastanın 503'ü inoperabl mide kanseri kabul edilmiş, medikal tedavi amacıyla onkolojiye yönlendirilmiştir. Kalan 1006 hastaya laparatomi ve/veya gastrektomi yapılmıştır. Laparatomi yapılanların 61'inde (%5.4) patolojik olarak erken mide kanseri saptanmıştır.* ***Sonuç:*** *Gastrik kanserli hastalar arasında erken mide kanseri olan olgu sayımız, Japonya ve diğer batılı ülkelerden daha az olarak bulunmuştur. Birçok batılı ülkede olduğu gibi tarama endoskopileri ülkemizde de maliyetli olmaktadır. Ancak alarm semptomları olan hastalarda boyama endoskopileri ve magnifiye endoskopi kullanılması erken mide kanseri tespit oranını yükseltecektir.*

Anahtar kelimeler: Erken mide kanseri, kromoendoskopi, endoskopik submukozal disseksiyon

Address for correspondence: Hüsnü Oğuz KOÇ
S.B. İstanbul Eğitim ve Araştırma Hastanesi,
Genel Cerrahi Kliniği, İstanbul, Turkey
Phone: + 90 212 661 81 28 • Fax: + 90 212 661 88 95
E-mail: oguzcoach@yahoo.com

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INTRODUCTION

The Japanese Gastric Cancer Association has defined early gastric cancer (EGC) as tumor invasion confined to the mucosa or submucosa, regardless of the presence of regional lymph node metastasis (1). Radical surgery, with complete removal of the first- and second-tier lymph nodes, has become the standard treatment for patients with EGCs. The incidence of lymph node metastasis in patients with intramucosal and submucosal EGCs has been reported as approximately 3% and 20%, respectively (2). The five-year survival rates in Japanese patients with intramucosal and submucosal invasive cancers were reported as 99% and 96%, respectively (3). Every year, approximately 10,000 patients in Japan are newly diagnosed with EGC using histochemical methods and optical chromoendoscopy during routine screening endoscopies, constituting 50% of all Japanese patients with gastric cancer (4). In western countries, however, only about 20% of patients newly diagnosed with gastric cancer have EGC. In Japan, many patients with EGC are treated with minimally invasive techniques of endoscopic submucosal dissection (5). Diagnosis in the early stages is important in choosing a treatment method and in achieving longer survival. Unfortunately, the prognosis of patients with advanced gastric cancer is poor. Late diagnosis is due primarily to late admission of patients or overlooked EGCs in early endoscopies.

In Turkey, there is no detailed database regarding the rate of EGC relative to the number of patients with gastric cancer. We therefore retrospectively reviewed the results of all gastroscopic evaluations in our clinic over a nine-year period. We assessed treatment methods and outcomes of all patients diagnosed and treated for gastric cancers, including EGC.

MATERIALS AND METHODS

All gastroscopic reports conducted in our hospital between January 2000 and January 2009 were accessed via a digital archive. All patients endoscopically diagnosed with gastric cancer were identified and their histological reports were collected. We excluded all patients showing discrepancies between endoscopic and histopathological diagnoses. Subsequent files of all patients admitted to surgical clinics were also identified and examined.

Patients were divided into two groups as those who underwent gastroscopy in 2000–2004 and those who underwent gastroscopy in 2005–2009. For each time period, we recorded the total number of gastroscopies, the total number of patients with endoscopically and histopathologically proven gastric cancer, the total number of patients with EGC and advanced gastric cancer, the total number of patients with inoperable gastric cancer, and the total number of laparotomies. The age and gender of all patients with EGC (Tables 1, 2), the macroscopic type of tumor (Table 3), its localization in the stomach (Table 4), the type of surgery (Table 5), the histopathological verification of the tumor, lymph node involvement, and the general state of the patients were examined and recorded. Table 3 shows macroscopic tumor classification in the stomach, whereas Table 4 shows tumor localization in the stomach.

Continuous variables are reported as mean and standard deviation and categorical variables as percentages. The differences between gender, type of operation, type of tumor, and tumor localization between the two periods were evaluated using the x^2 test, with statistical significance set at $p<0.05$ (bidirectional).

Table 1. Mean patient age in early gastric cancer patients

Age (years)	2000–2004	2005–2009
Female	63.3 (38–85)	69.5 (42–82)
Male	59.3 (35–80)	67.4 (39–86)
Mean	60.6 (35–85)	68.3 (39–86)

Table 2. Gender distribution* in early gastric cancer patients

	2000–2004	2005–2009
Total number	21	61
Female	7 (33.3%)	23 (37.7%)
Male	14 (66.6%)	38 (62.3%)

*x^2= 0.87, p=0.34. Difference according to gender between the two periods was not significant.

Table 3. Macroscopic tumor classification in early gastric cancer patients

Tumor type	2000–2004	2005–2009
Type I (protruded)	2	9
Type IIa (superficial elevated)	8	19
Type IIb (superficial flat)	3	10
Type IIc (superficial depressed)	5	13
Type III (excavated)	3	10
Total	21	61

RESULTS

Of the 15,174 gastroscopies performed in the endoscopy unit of our hospital during 2000–2004 (first period), 536 patients (3.5%) were diagnosed with gastric cancer. Of the 22,594 gastroscopies performed between 2005 and 2009 (second period), 973 patients (4.3%) were diagnosed with gastric cancer. Overall, during this nine-year period, gastroscopies were performed on 37,768 patients, of whom 1,509 (4%) were diagnosed with gastric cancer. Of the 536 patients diagnosed with gastric cancer in 2000–2004, 150 (28%) were considered inoperable on radiological and other examinations; these patients were transferred to the Oncology Department for medical treatment. The remaining 386 (72%) underwent laparotomy and/or radical surgical intervention, with only 21 of these patients (3.9%) diagnosed with histopathologically proven EGC. Of the 973 patients diagnosed with gastric cancer in 2005–2009, 353 (35.2%) were found to be inoperable and transferred to the Oncology Department for chemotherapy. The remaining 620 patients (63.8%) underwent laparotomy and/or radical surgery, with 61 (6.3%) of these patients diagnosed histopathologically with EGC. During this nine-year period, 82 patients (5.4%) were diagnosed with EGC.

Macroscopic tumor classification is shown in Table 3. The most frequent tumor type in our series was type III.

Table 4. Tumor localization in the stomach in early gastric cancer patients

Tumor localization	2000–2004		2005–2009	
	F	M	F	M
Antrum	3	9	10	15
Lesser curvature	2	3	9	8
Greater curvature	2	-	2	3
Cardia	-	2	2	11
Remnant	-	-	-	1

* x^2= 0.01, p=0.87 Difference according to gender between the two periods was not significant. F: Female; M: Male.

Table 5. Type of surgery in early gastric cancer patients

Operation	2000–2004	2005–2009
Total gastrectomy	13 (9M, 4F)	50 (36M, 14F)
Subtotal gastrectomy	8 (5M, 3F)	11 (2M, 9F)

* x^2=0.01, p=0.87 for total gastrectomy. x^2=2.23, p=0.13 for subtotal gastrectomy. Differences according to gender between the two periods were not significant.

All patients with EGC underwent D2 dissection and were postoperatively diagnosed with differential adenocarcinoma. During the first time period (2000–2004), 19 ± 4 lymph nodes were removed from 21 EGC patients. Histopathological examination of these lymph nodes revealed perigastric lymph node metastasis in 4 (19%) and reactive hyperplasia in 16 (81%) patients. Two of the patients with perigastric lymph node metastasis were positive for type IIc and 2 for type III macroscopic lymph nodes. During the second time period (2005–2009), an average of 22 ± 6 lymph nodes were removed from the 61 patients with EGC. Histopathological examination showed perigastric lymph node metastasis in 14 (22.9%) and reactive hyperplasia in 47 (77.1%) patients. Of the 14 patients with perigastric lymph node metastasis, 5 were positive for type IIc and 9 for type III.

Of the 21 EGC patients who underwent surgery in 2000–2004, 17 were followed up; of these, 5 (29.4%; 2 females, 3 males) survive to date, whereas 12 died at a median 36 months (range: 18–52 months) after the operation as a result of complications related to their disease. All patients with lymph node positivity died. Of the 61 patients who underwent surgery within the second period (2005–2009), 54 were followed up; of these, 48 (88.9%; 26 females, 22 males) survive to date. Of the 6 patients who died, 4 died at a median of 24 months (range: 17–30 months) after surgery from complications related to cancer, whereas the other 2 died 9 and 12 months after surgery due to myocardial infarctions. All patients who died had lymph node positivity.

DISCUSSION

Although the incidence of gastric cancer is decreasing in many countries, it remains one of the most common cancers and the second most common cause of cancer deaths worldwide (6). Outside Japan, survival rates for patients with gastric cancer remain poor, with an estimated five-year survival rate in Europe of only 24–27% (7). The survival rates in North America are somewhat better, perhaps owing to the overall larger numbers of diagnostic endoscopic procedures performed, leading to earlier detection (7). In Japan, where population-based endoscopic screening was introduced in the 1960s, the five-year survival is greater than 50% for patients with gastric cancer (7,8). The poor prognosis of patients with gastric cancer is due to late presentation during the natural history of

the disease, with local extension or metastatic disease rendering the condition inoperable. For example, about 90% of patients with gastric cancer in western countries are considered unsuitable for surgery at the time of presentation. This is in contrast to Japan, where EGCs comprise 50% of gastric cancers detected (9,10).

Screening programs are not feasible in European and other western countries; hence, gastric cancer is usually diagnosed when the patient is admitted to the hospital with symptoms. Patients presenting with these "alarm symptoms", including weight loss, dysphagia, upper gastrointestinal bleeding, deep anemia, and anorexia, are advised to undergo endoscopic examination without delay. However, patients with symptoms that result from gastric cancer often present with more advanced tumors (6,10,11).

Age and gender are important factors in the development of gastric cancer. Although the risk of gastric cancer increases with age, there is no determined cut-off age. However, gastric cancer appears more commonly in patients aged at least 50 years (6). In addition, gastric cancer is more common in men than in women. Even considering all selection criteria, including alarm symptoms, gender and age, it may be difficult to differentiate EGC symptoms from those of dyspeptic complaints (6).

Patients usually undergo upper gastrointestinal endoscopy for dyspeptic complaints, with about 50% showing no organic cause (12,13). It is important to detect cancer during endoscopy. For example, slight changes in the color of the mucosa (more pale or red spaces), irregular microvascular structures, or slightly elevated or depressed spaces should be recognized (14). In western countries, white-light endoscopy systems are often used, and diagnosis of premalignant lesions with these endoscopes is quite difficult. In contrast, the Japanese have been instrumental in the adoption of technologies to enhance the detection of EGC, including the use of high-resolution and magnification endoscopy, chromoendoscopy, point spectroscopy, fluorescence imaging, and confocal endoscopy (15,16). Endoscopy units in western countries often use chromoendoscopy, together with indigo carmine dye, which accentuates mucosal patterns, helping to identify distorted surface topography (14,17,18).

Endoscopic submucosal dissection has become the standard in the treatment of EGC, especially in Japan (19,20). Differentiated nonulcerative lesions up to 3 cm in diameter can be removed using this technique. In many respects, endoscopic resection is comparable to conventional surgery, with the advantages of being less-invasive and more cost-effective. The extremely low incidence of lymph node involvement in certain stages of EGC means that cure can be achieved with such local treatment in selected patients. Endoscopic resection allows complete pathological staging of the cancer, which is critical in stratifying patients and selecting further treatment (21,22).

Our patients were examined by standard white-light endoscopy, and chromoendoscopy was not performed. Thus, our rate of EGC diagnosis was lower than that in western countries and Japan. Over a nine-year period, 5.4% of our patients with gastric cancer had EGC, 3.9% in 2000–2004 and 6.3% in 2005–2009. All patients with EGC were treated with radical surgery; none underwent less-invasive surgery or an endoscopic method. EGC was commonly localized to the antrum. The incidence of lymph node metastasis was higher in patients with macroscopic types IIc and III lesions. Although the number of our patients was small, overall survival was longer in patients without lymph node metastasis. Our previous study on *Helicobacter pylori (HP)* positivity, an important factor in gastric cancer etiology, during the period 1995–2004, showed that the rate of HP positivity was 61.5% in 1995–1999 and 38.47% in 2000–2004 (23). Compared with Turkey, the HP positivity rates are lower in Japan and developed western countries (24,25), although the incidence of EGC is higher in these countries. Therefore, the rate of EGC diagnosis was lower than expected in our series. As in other western countries, screening endoscopy is not feasible in Turkey. Therefore, patients with alarm symptoms or in risk groups should undergo endoscopic evaluation using systems allowing high-quality digital imaging. These systems must be easily accessible and inexpensive, and simple chromoendoscopy is required in routine daily use. Furthermore, patients with EGC should be treated with less-invasive methods, including endoscopic submucosal dissection and less-invasive laparoscopic surgery.

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