Early gastric cancer: endoscopic mucosal resection

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Abstract

In Japan, endoscopic mucosal resection (EMR) is now accepted as a treatment option for cases of early gastric cancer (EGC) with minimum probability of associated lymph node metastasis. In National Cancer Center Hospital (NCCH), EMR is currently applied to patients with early cancers up to 30mm diameter that were of intestinal type, and were superficially elevated and/or depressed (Type I, IIa and IIc) but without ulceration or definite signs of submucosal invasion.

Four hundred seventy nine lesions of EGC in 449 patients were treated by EMR from 1987 through 1998. Submucosal invasion was found on subsequent pathologic examination in 74 lesions, and surgery was recommended. Sixty nine percent of intramucosal cancer was resected with a clear margin, which was therefore judged to be a "complete resection".

Local recurrence in the stomach occurred in 2% (5 lesions) with complete resection and in 17% (18 lesions) without complete resection treated conservatively or endoscopically, and all were subsequently treated with curative intent. There were no gastric cancer-related deaths for a median follow-up period of 38 months (3-120 months). Bleeding and perforation were two major complications in EMR, but there were no treatment-related deaths.

We believe that EMR allows us to perform less-invasive treatment without sacrificing the possibility of cure. We hope to promote its use around the world.

Key words: Endoscopic mucosal resection, early gastric cancer.

Introduction

Early gastric cancer (EGC) is defined as that confined to the mucosa or submucosa regardless of the presence or absence of regional lymph node metastases (1). A steady increase of EGC was observed by the nationwide data collection of gastric cancer patients in Japan (2), so as a National Cancer Center Hospital (NCCH) as shown in Fig. 1. The present rate of EGC is approximately 50% of all resected cases of gastric cancer, and the 5-year survival rate of patients with EGC is over 90% after gastrectomy with complete removal of primary and secondary lymph nodes (3, 4). Endoscopic mucosal resection (EMR) for EGC was firstly introduced in 1984

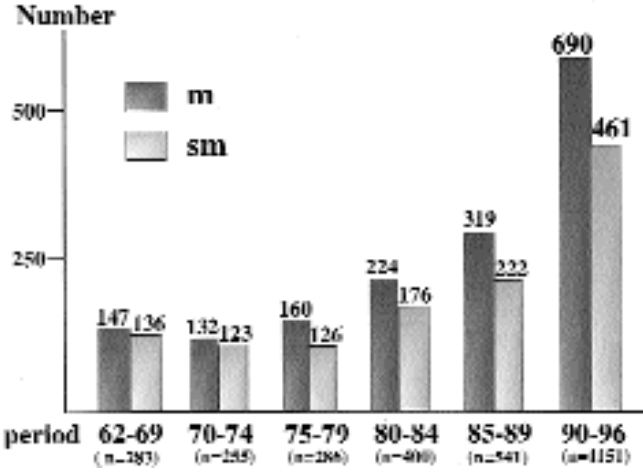

Fig. 1.: Trends of early gastric cancer treated at National Cancer Center Hospital. m; intramucosal cancer, sm; submucosal cancer.

Riassunto

NEOPLASIA GASTRICA IN STADIO PRECOCE: REZIONE ENDOSCOPICA

In Giappone la mucosectomia endoscopica (EMR) rappresenta un'opzione di trattamento riservata ai casi di early gastric cancer a basso rischio di metastasi linfonodali. Presso il National Cancer Center Hospital (NCCH), l'EMR viene correntemente impiegata nel trattamento di pazienti con neoplasia in stadio precoce con diametro 30mm, istotipo intestinale, a superficie elevata e/o depressa (Tipo I, IIa e IIc), ma senza ulcerazione né chiari segni di invasione sottomucosa. Dal 1987 al 1998 sono state trattate mediante EMR 479 lesioni di EGC in 449 pazienti. In 74 casi è stata documentata all'esame istologico l'invasione della sottomucosa e, pertanto, è stato eseguito un intervento chirurgico di gastroresezione. Nel 69% delle lesioni intramucose le resezioni endoscopiche sono state effettuate su mar -

gine sano e, pertanto, giudicate come resezioni complete. Una recidiva locale gastrica è stata osservata nel 2% dei casi (5 lesioni) trattati mediante resezione completa e nel 17% dei casi (18 lesioni) sottoposti a resezione endoscopi - ca non completa, tutti successivamente trattati con intento curativo. Ad un follow-up medio di 38 mesi (3-120 mesi) non è stato documentato alcun decesso correlato alla neo - plasia. Le due principali complicanze della metodica sono state il sanguinamento e la perforazione gastrica che non hanno comportato alcuna mortalità.
È nostra opinione che l'EMR sia in grado di offrire, in caso di neoplasia precoce, le stesse possibilità di cura dell'intervento chirurgico attraverso una metodica a bassa invasività e riteniamo, pertanto, che il suo impiego possa essere esteso anche al mondo occidentale.
Parole chiave: mucosectomia endoscopica-early gastric can - cer.

Tab. I - MACROSCOPIC TYPE AND LOCATION OF EARLY GASTRIC CANCER RESECTED BY EMR

	L	*M*	*U*	*Total*
0-I type (protruded)	6	5	4	15
0-IIa type (superficial elevated)	75	76	33	184
0-IIc type (superficial depressed)	150	85	45	280
	231 (48%)	**166** (35%)	**82** (17%)	**479**

in Japan (5, 6), and now is generally accepted as a therapeutic option for the management for EGC.
In this article, we evaluate and discuss the present situation of EMR for EGC, sbowing our results at NCCH.

Indications of EMR

EMR is a minimally invasive procedure, but is only a local treatment without lymph node dissection. Therefore, indications of EMR are determined by the risk of lymph node metastasis (7), and endoscopic techniques. The incidence of metastasis of intramucosal EGC has been reported to be approximately 3%, and is 20% in submucosal EGC (3, 4, 7, 8). To clarify the characterestics of patients having lymph nodal metastasis, we investigated 1196 patients patients with solitary intramucosal EGC who underwent resection at NCCH (7). Multivariate analysis revealed that lymphatic vessel invasion, histologic ulceration of the tumor, and larger tumor diameter (30mm) were independent risk factors for regional lymph node metastasis. The incidence of lymph node metastasis from intramucosal EGC that is negative for these risk factors was only 0. 36%, which is lower than the mortality rate in operation for EGC (about 0.5% at NCCH).
Therefore, we think lymphadenectomy is not necessary for these patients.
Current indications for EMR at NCCH include all of the following: 1. Intestinal histological type. 2. Superficial, elevated or depressed macroscopic appearance (Types I, IIa, IIc). 3. No ulceration. 4. Diameter 30mm. and 5. No apparent invasive findings (9). When EMR was introduced to NCCH in 1987, the indication size was 15mm or less in diameter. However, it was increased to 30mm based on a review of resected intramucosal cancer and the development of endoscopic techniques and equipment. Since it is sometimes difficult to accurately assess the depth of invasion prior to EMR, we are prepared to remove any lesion that appears to be confined to the mucosa if it meets the other criteria. Since endoscopic ultrasonography is not sensitive enough to evaluate minute invasion to the submucosa, we do not use it routinely. EMR is a therapeutic option, and its indications should be also determined in comparison to other procedures and the patient's condition.

Evaluation of resected specimens

The resectability of EMR specimens was carefully evaluated both endoscopically and histopathologically in slices at 2 mm intervals according to the "Japanese Classification of Gastric Carcinoma" (10). Our current definition of "high probability of cure" includes all of the following: 1. Intramucosal cancer. 2. Intestinal histological type. 3. No histological ulceration. 4. No lymphatic or venous invasion. and 5. No tumor invasion to the lateral margin. Among them, Nos. 1-4 are indispensable for low probability of regional lymph node metastasis, and No. 5 is important as a risk factor of local recurrence. Since submucosal invasion and/or vessel involvement are regarded to be associated with a high risk of positive nodes or distant metastasis, intervention was strongly recommended in such cases.
Evaluation of invasion to the lateral margin was classified into the following three groups merely for convenience in view of endoscopic and histopathologic confirmation, while it was sometimes difficult. After resection in multiple fragments, resectability was evaluated based on completely reconstructed specimens (Fig. 2).
1. Complete resection: When the lateral margin was clear endoscopically and pathologically (low probability of local recurrence)
2. Incomplete resection: When the tumor definitely invaded to the lateral margin endoscopically and pathologically (high probability of local recurrence)
3. Not evaluable: When the tumor was removed endo-

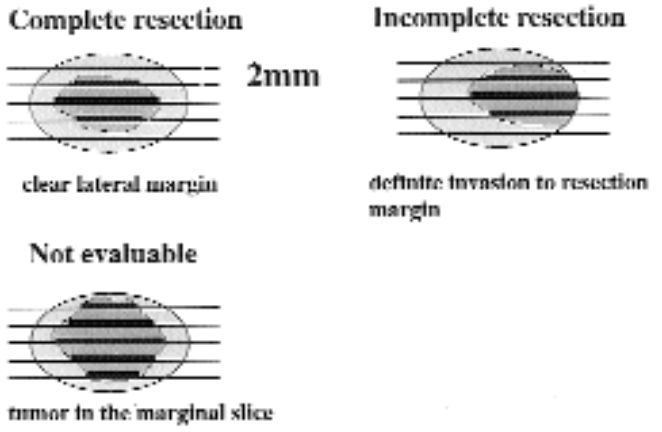

Fig. 2.: Histopathological evaluation of resected specimens.Three schemes show definition of resectability in this article (see text).

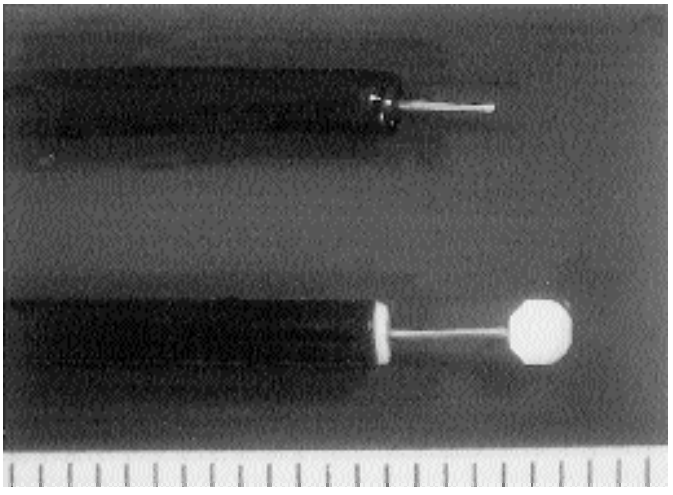

Fig. 3.: top; a needle knife. bottom; Hosokawa's knife (Insulated-tipped knife). A round ceramic ball is tipped at the top of needle knife.

scopically, but its lateral margin was not pathologically evaluable due to a burn effeat, or mechanical damage, or when reconstruction was difficult due to a multi-fragment resection.

Procedures

The so-called "strip biopsy method", a relatively simple technique that has been described elsewhere(5, 6), is most common. We think that single-fragment resection is referable, because with multi-fragment specimens it is often difficult to reconstruct the entire lesion. There have been a number of reports on the EMR procedure to resect larger lesions safely (11, 12). From 1997, we often use a new EMR procedure using an insulation-tipped diathermic knife (Hosokawa's knife, Fig. 3), which was developed by Hosokawa at our hospital in 1995 (13). EMR procudure using Hosokawa's knife is demonstrated in Fig. 4.

Results of EMR for EGC in NCCH

Four hundred seventy nine EGCs in 449 patients were treated for cure using EMR from 1987 through 1998. Mean age of the patients was 67.6 years and the sex ratio was 4.13. The treated lesions consisted of 413 solitary, 17 double, 1 triple, 1 quadruple, and 13 metachronous solitary EGCs.

As shown in Table 1, the half of treated lesions were situated in the lower third of the stomach, while 58% was of the superficial depressed type (O-IIc). About 90% was less than 20mm in diameter.

The clinical courses of all of the patients are shown in (Fig. 5). Thirty of 74 cases with submucosal invasion

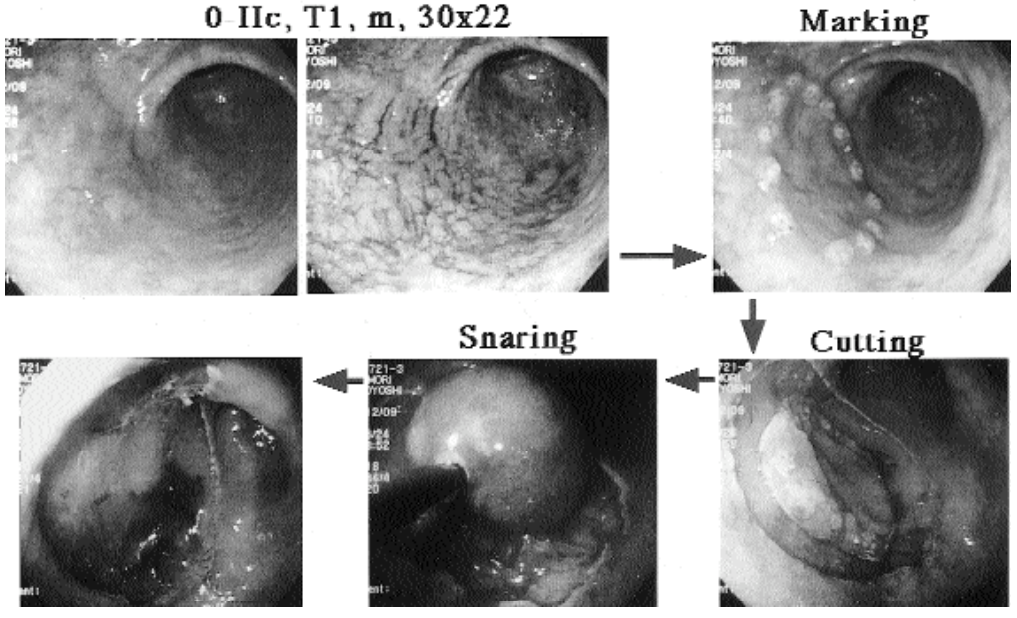

Fig. 4.: Procedure of EMR using Hosokawa's knife. After marking, the lesion was cut around by the knife, snared and resected.

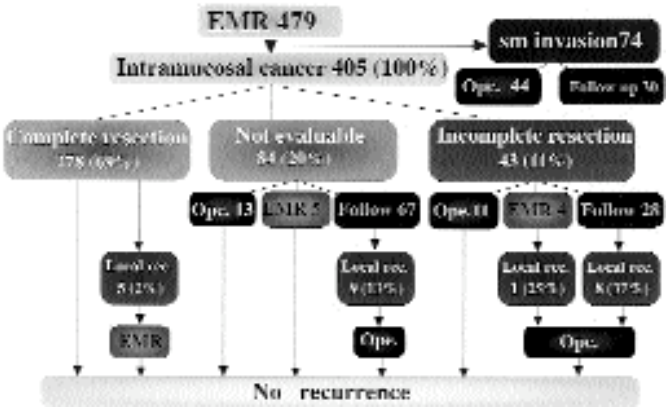

Fig. 5.: Clinical courses after EMR for early gastric cancer.

were merely followed because of minute submucosal invasion, advanced age, other diseases or the patient's refusal of an additional operation.
Of 278 lesions of "complete resection", 2% had local recurrence, and all were subsequently treated with curative intent. The rest are disease-free at a median follow-up period of 38 months. Of 127 lesions without "complete resection", 33 were treated by an additional operation or endoscopic therapy, while the rest were followed intensively. Among the 104 lesions which were treated conservatively or endoscopically, there were 18 local recurrences after a median follow-up of 4 months. All of the patients eventually underwent surgery and are free from the disease.

Follow-up program

A follow-up program is important for finding local recurrence and other cancer in the stomach (8).
The incidence of multiple primary lesions in surgically treated EGC was around 10% at NCCH, and surprisingly one third of secondary lesions were missed in an initial endoscopic examination (14). The stomach may also contain premalignant conditions such as intestinal metaplasia, we should pay attention not only to recurrence but also to other cancer in the stomach.
We perform follow-up endoscopy at 3 and 6 months after EMR in the first year, and yearly thereafter.

Complications

Bleeding and perforation were two major complications in EMR. All bleeding was amenable to endoscopic treatment with ethanol injection, clipping, and spraying of thrombin solution in the stomach. There were 25 cases of perforation (5.2%), the first four were converted to open surgery. Since then, all perforations have been succesefully treated with endoscopic clipping.

EMR vs. surgical local treatment for intramucosal cancer

EGC with low probability of lymph node metastasis is the most suitable candidate for both EMR and local resection. Considering QOL (quality of life) of patients and cost, there seems to be no doubt that EMR is more superior than surgical treatment. Therefore EMR is basically chosen as treatment for EGC in our hospital, and surgical resection is done when EMR is technically difficult. Since developments have occurred in EMR procedures and laparoscopic surgery, it is time to discuss which procedure is appropriate for the management of EGC.

Conclusions

The EMR technique has bean developed mainly in Japan where there is a high incidence of EGC, but it is used infrequently in the West. Our results revealed that EMR can provide the same favorable long-term survival rates as traditional therapy, as long as the criteria are strictly respected. The proportion of EGC cases treated by EMR at NCCH has risen, and this accounted for about 40% of all EGC cases in 1998. EMR is now the treatment of choice for mucosal EGC and we hope to promote its use around the world.

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