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EUS in the Management of High-Risk Gastrointestinal Precancerous Lesions before Endoscopic Resection

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Abstract

Aim: To investigate the evaluation of EUS for the high-risk gastrointestinal precancerous lesions (HRGIPCL) before endoscopic resection.

Methods: The patients with HRGIPCL scheduled for endoscopic resection, were randomized to preoperatively performing EUS (Group A) versus without EUS (Group B). Data were prospectively collected as follows: routine endoscopic results, EUS findings, therapeutic maneuvers, resected lesion size, final diagnosis and the grades of therapeutic maneuvers.

Results: 116 patients with 156 HRGIPCL were included in Group A and 116 with 140 HRGIPCL in Group B. In terms of routine endoscopic results, resected lesion size (1.84 ± 1.30cm in Group A vs 1.70 ± 0.97cm in Group B) and final diagnosis, no differences were found between two groups (P >0.05). 207 endoscopic mucosal resection (EMR) was performed for 157 patients (114 EMR for 81 patients in Group A vs 93 for 76 in Group B), 14 endoscopic piecemeal mucosal resection (EPMR) for 14 patients (7 in Group A vs 7 in Group B), and 72 endoscopic submucosa dissection (ESD) for 67 patients (32 ESD for 30 patients in Group A vs 40 for 37 in Group B). No significant differences were observed between two groups (P >0.05). 33 adverse events occurred with significant differences between two groups (11 in Group A vs 22 in Group B, P < 0.05). The grades of therapeutic maneuvers in Group A was higher than that in Group B (P < 0.05).

Conclusion: It was helpful to be evaluated by EUS for HRGIPCL before endoscopic resection.

Key Words: *endoscopic ultrasonography; high-risk; gastrointestinal; precancerous lesions; low grade intraepithelial neoplasia; laterally spreading tumor; large gastrointestinal adenoma; endoscopic mucosal resection; endoscopic piecemeal mucosal resection; endoscopic submucosa dissection*

INTRODUCTION

We can find the early gastrointestinal cancer and remove it through endoscopy [1–8], Can we nip in the bud, blocking the early cancer at the precancerous stage [9]?

It is a common treatment option to endoscopically find and remove the high-risk gastrointestinal precancerous lesions (HRGIPCL), for example, low grade intraepithelial neoplasia (LGIN), laterally spreading tumor (LST) and large gastrointestinal adenomas. Will endoscopic ultrasonography (EUS) be helpful preoperatively? Because, as we all know, it was usually helpful for the early malignant lesions to be valuated using EUS before endoscopic removal [10–13].

MATERIALS AND METHODS

Patients

From April 2009 to March 2015, the patients with HRGIPCL scheduled for therapeutic endoscopic intervention, were randomized to preoperatively performing EUS (Group A) versus no EUS (Group B). Based on our clinical experiences and the relevant literatures [9,14–16], we classified the following lesions as HRGIPCL: LGIN, LST (>1.0 cm), sessile or rebagliati polyps (limited to tubular, tubulovillous and villous adenomas, >1.0 cm). All the lesions had undergone routine endoscopy, biopsy and histopathological examination, and the malignant ones including high grade intraepithelial neoplasia (HGIN) had been excluded from the study. This study got the approval from Weihai Municipal Hospital Ethics Committee. After each patient signed an informed consent, each endoscopic exploration began.

Procedures

All the endoscopic procedures were carried out by four endoscopists, assisted by three nurses. EUS was performed with a radial echoendoscope (Olympus GF-UM2000, Olympus Medical Systems Corp, Tokyo, Japan). Therapeutic endoscopic intervention were done using gastroscopy, colonoscopy, snare, single use electrosurgical knife [including IT Knife 2 (KD-611L), Hook Knife (KD-620LR), Dual Knife (KD-650L) and Triangle Tip Knife (KD-640L), Olympus Medical Systems Corp, Tokyo, Japan)], or Hybrid Knife (ERBE Elektromedizin GmbH, Tuebingen, Germany). ERBE VIO 200D (ERBE Elektromedizin GmbH, Tuebingen, Germany), was used as Electrosurgical Generator.

All the endoscopic explorations were conducted under intravenous anesthesia administered by two anesthesiologists: intravenous fentanyl and midazolam followed by propofol.

Data were prospectively collected as follows: age, sex, routine endoscopic results, EUS findings, therapeutic maneuvers, resected lesion size, final diagnosis, the grades of therapeutic maneuvers, and endoscopic complications.

Statistical analysis

Quantitative variables were described as mean ± standard deviation. Kolgomorov-Smirnoff test was used to verify the normal distribution of quantitative data, and T-test was used for testing significance between quantitative variables. Chi-square test was used to detect significant difference among qualitative variables. The *P*-value under 0.05 was considered significant.

RESULTS

General information

116 patients were included in Group A and 116 in Group B. In terms of age, sex and preoperatively routine endoscopic results, no differences were found between two groups (P >0.05). The above data were shown in Table 1.

Table 1. General information

	Group A	Group B	*P*-value
Total	116	116	
Gender			0.130
Men	70	81	
Women	46	35	
Mean age (years)	61.66 ± 10.10	59.08 ± 10.91	0.062
Indication (Number of patients/ lesions)	116/156	116/140	0.537
Location of lesion			0.523[a]/0.233[b]
Esophagus	0/0	1/1	
Stomach	23/25	24/27	
Duodenum	0/0	2/2	
Large intestine	93/131	89/110	
Pattern of Lesion			0.299[a] /0.517 [b]
LST	37/42	32/36	
Sessile	74/100	81/96	
Rebagliati	13/14	7/8	
Preoperative pathology of Lesion			0.097[a] /0.068 [b]
LGIN	34/38	40/41	
Tubular adenomas	47/67	59/70	
Tubulovillous adenomas	40/50	27/29	
Villous adenomas	1/1	0/0	

LST: laterally spreading tumor; LGIN: low grade intraepithelial neoplasia
[a]: *P*-value according to the number of patients; [b]: *P*-value according to the number of lesions

Therapeutic maneuvers, resected lesion size and final diagnosis

207 endoscopic mucosal resection (EMR) was performed for 157 patients (114 EMR for 81 patients from Group A vs 93 for 76 from Group B), 14 endoscopic piecemeal mucosal resection (EPMR) for 14 patients (7 in Group A vs 7 in Group B), and 72 endoscopic submucosal dissection (ESD) for 67 patients (32 ESD for 30 patients belonging to Group A vs 40 for 37 belonging to Group B). There were no significant differences (P = 0.398>0.05). According to the preoperative EUS findings, 3 patients preferred surgical operation rather than planned endoscopic removal in Group A.

The mean size of resected lesions was 1.84 ± 1.30cm in Group A and 1.70 ± 0.97cm in Group B, without significant differences (P = 0.293> 0.05).

According to pathological diagnoses of removed specimens, including surgical specimens, final diagnoses were shown in Table 2. There were no significant differences between two groups (P = 0.096 > 0.05).

Grades of therapeutic maneuvers

On the basis of the principle, that is, it was helpful for the gastrointestinal early malignant lesions to be evaluated by EUS before endoscopic resection, we developed a scoring system as shown in Table 3. According to this scoring system, the grades of therapeutic maneuvers in Group A was higher than that in Group B (P = 0.000 < 0.05). The above data were shown in Table 4.

Table 3. The scoring system of therapeutic endoscopic maneuvers for HRGIPCL

	Grades according to postoperative pathology			
	Benign lesions	HGIN	Early cancer	Advanced cancer
Evaluation by EUS	0	1	2	3
Without evaluation by EUS	0	0	0	0

HRGIPCL: high-risk gastrointestinal precancerous lesions;
HGIN: high grade intraepithelial neoplasia

Table 4. Grades of therapeutic endoscopic maneuvers for HRGIPCL in two groups

	Grades /Number					*P*-value
	Benign lesions	HGIN	Early cancer	Advanced cancer	Total	
Group A	0/125	1/27	2/2	3/2	37/156	0.000
Group B	0/114	0/19	0/5	0/2	0/140	

HRGIPCL: high-risk gastrointestinal precancerous lesions;
HGIN: high grade intraepithelial neoplasia

Adverse events

5 cases of endoscopic procedures followed by appended surgery which included 1 early signet ring cell cancer from Group A, 2 early cancer with suspicious residual tumor and 2 advanced cancer from Group B.

28 cases of endoscopic complications included 16 bleeding (6 in Group A and 10 in Group B), and 12 perforation (4 in Group A and 8 in Group B). 1 bleeding in Group B, and 3 perforation(1 in Group A and 2 in Group B) underwent surgical operation.

In terms of complications, no significant difference were observed between the two groups ($P = 0.058 > 0.05$). However, 11 adverse events in Group A were less than 22 in Group B ($P = 0.018 < 0.05$).

DISCUSSION

Generally, EUS had better to be performed before the endoscopic resection is carried out for the early gastrointestinal cancer. Though, EUS is not usually required prior to the endoscopic removal for HRGIPCL. This is maybe due to that HRGIPCL is often considered as benign lesions by endoscopists with preconceived ideas. In fact, the so-called HRGIPCL may be just the tip of the iceberg [9,14]. May EUS be helpful before the therapeutic endoscopic procedures for HRGIPCL?

In our study, 46 HGIN and 11 gastrointestinal cancers were finally found in the 296 preoperative so-called HRGIPCL. Moreover, of these 11 cancers, there were 4 advanced cancers (2 from Group A and 2 from Group B). Some studies had similar findings. O'Brien MJ et al found HGIN among 35% of colorectal villous adenomas (>1 cm) [17]. Moreover, of 43 colorectal adenomas(≥2.5 cm), Elizabeth D. Euscher et al observed 5 invasive carcinoma [14].

In the Group B, these 2 advanced colorectal cancers preoperatively appeared as one LST and one sessile tubulovillous adenomas. Both of them underwent the surgery following the failed ESD. Moreover, in the Group B, one gastric early cancer after ESD and one colorectal cancer after EPMR, both accepted appended surgery because the cancer cells were observed on bottoms of resected lesions. Though, no cancer tissue were found in the postoperative specimen. However, the gratified results were observed in the Group A. Based on the preoperative EUS findings, those 2 advanced colorectal cancers being formerly regarded as sessile tubulovillous adenomas, both preferred to the surgery instead of the endoscopic resection.

Furthermore, there was such a surprised case in the Group A. One LGIN at the anterior wall of the junction of gastric body and antrum, was found by the gastroscope in his health check. A month later, he accepted the second gastroscopy, and the previous lesion area seemed to return to normal. EUS was still performed in accordance with the established procedures. The thickened hypoechoic mucous layer, with the incomplete muscularis mucosa and submucosa, was observed. Then, the jumbo biopsy was finished, and its histopathologic behaviors showed the moderately differentiated mucinous adenocarcinoma infiltrating into the submucosa. The final surgical specimens displayed the same pathological diagnosis and no lymph node metastasis.

Additionally, a large rectal LST in Group B, gave us a profound lesson. During the process of ESD, injection bleeding occurred, and endoscopic hemostasis failed, leading to hypovolemic shock, and following by surgery, because of a thick vascular broken end. In fact, ultrasonography preoperatively found a suspicious blood vessel within the thickening rectal mucosa. Unfortunately, it did not attract our enough attentions. We usually thought a crude vessel in bulky pedicle polyp. This lesson told us that EUS help to discovery the coarse vascellum hiding in the lesion, regardless of its shape, thus avoiding uncontrollable intraoperative bleeding.

However, we have to acknowledge the shortcomings of EUS [18–20]. It can usually reveal whether the cancer has invaded the muscularis propria. That is, it can distinguish the early gastrointestinal cancers from the advanced ones. Though, EUS is difficult to accurately define the depth of tumor reaching in the submucosa. So, before ESD for early cancer, if EUS says "NO", we can choose to believe EUS, and if EUS says "YES", we can choose to doubt EUS [21,22]. Before the endoscopic removal for early cancer, it is primary to preliminary screen the early cancers and advanced ones out from HRGIPCL. Obviously, EUS is qualified for this task, though the procedures and findings of EUS are all fairly subjective.

At the same time, many studies have shown that, the mucosal microstructure including the pit pattern and microvascular pattern demonstrated by chromoendoscopy and magnifying endoscopy, was very helpful to determining early gastrointestinal cancer, and identifying some early cancers suitable for endoscopic resection [23–28]. However, at present, this approach was mainly applied to esophageal cancer. It was still difficult to be used for gastric cancer and colorectal cancer. Even so, in fact, we had not yet mastered this method well. In order to be proficient in this means, it was necessary to carefully observe a large number of early gastrointestinal cancers by chromoendoscopy and magnifying endoscopy. Therefore, we thought that it was more difficult to master this method than to apply EUS for evaluating the gastrointestinal cancers. Apparently, it would be better to combine these two methods.

In summary, our study showed that EUS could help reduce the incidence of adverse events during the endoscopic removal of HRG IPCL. Thence, we thought that it was helpful to be evaluated by EUS for HRGIPCL before endoscopic resection.

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Conflicts of interest: There are no conflicts of interest.

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