Endoscopic Intervention for Stomach Cancer

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Endoscopic intervention

- Bleeding control
- Stenting
- Ablation treatment
- Endoscopic resection (ESD)
Topics

• Brief history of gastric ESD in Korea
• Indications of ESD in Korea
• Outcomes of ESD for EGC
• How to teach and learn ESD?
History of gastric ESD in Korea

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The first report on EMR for EGC in Korea

EMR for adenocarcinoma: 19 cases

operation(+): 7 cases  operation(-): 12 cases
4 resection margin(+)
1 incomplete resection
2 F/U GFS, recur

surgical specimen  F/U gastroscopy

cancer(+) cancer(−) cancacr(+) cancer(−)
5 2 4 8

depth of burning poor surgical disease free
invasion effect condition: for 3~13 mo
m: 3 LC, burning
sm: 2 COPD, MM, effect: 2

(group A) (group B) (group C) (group D)

Lee JH. Korean J Gastrointest Endosc 1996;16:928-934
Early personal experience of gastric ESD (2005)
ESD for EGC in Korea
- From Nov 2011 – Dec 2014

• Number of ESD for EGC cases: 23,828
• Age: 64.9 +/- 9.9 years (median: 66)
• Male: female = 74.2% : 25.8%
• Hospital stay: 5.0 days
• Medical cost in 2014: 1,510,000 won (1,305 US dollars)
• Surgery within 3 months after ESD: 6.6%

Park CM. 24th KCHUGR Annual Scientific Meeting (2016-12-3)
Treatment of gastric cancer at SMC

Surgery
ESD

MERS outbreak in 2015

2012 2013 2014 2015 2016 2017 2018

2012 2013 2014 2015 2016 2017 2018

0 1000 2000 3000 4000 5000 6000 7000 8000 9000 10000 11000 12000 13000 14000 15000 16000 17000 18000

Surgery
ESD
Indications of ESD in Korea

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# Absolute and expanded indications

- **Traditional classification**

<table>
<thead>
<tr>
<th>Histology</th>
<th>Depth</th>
<th>M cancer</th>
<th>SM cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No ulceration</td>
<td>Ulcerated</td>
<td>SM1</td>
</tr>
<tr>
<td>Differentiated</td>
<td>≤ 20 mm</td>
<td>&gt; 20 mm</td>
<td>≤ 30 mm</td>
</tr>
<tr>
<td></td>
<td>A</td>
<td>B1</td>
<td>B2</td>
</tr>
<tr>
<td>Undifferentiated</td>
<td>C</td>
<td>D</td>
<td>D</td>
</tr>
</tbody>
</table>

- **A** absolute indication for ER
- **B** expanded indications for ER
- **C** expanded indications for ER
- **D** surgery (gastrectomy + lymph node dissection)
Absolute indication EGC by pre-treatment diagnostic groups

Pre-Tx AI EGC 396

ESD 355
LGD 1
HGD 4
AI EGC 229
BAI EGC 120
AGC 1
ESD 1
Surgery 53

Operation 41
LGD 1
AI EGC 29
BAI EGC 11
Surgery 1

Reason for surgery (multiple)
✓ Suspicious lymphadenopathy on CT (18)
✓ Multiple lesions (6)
✓ Patient’s wish (18)
✓ Difficult location (3)
✓ Suspicious SM invasion on EUS (2)

* BAI: beyond absolute indications

Lee JH. Surg Endosc 2016;30:3987-93
Standard indications of ESD in Korea

- ESD candidates are usually selected by the absolute indications.
- After ESD, expanded criteria is applied to determine whether the resection was curative.
- There are controversies about the safety of ESD for expanded indication cases.
Statement 1. Endoscopic resection is recommended for well or moderately differentiated tubular or papillary early gastric cancers meeting the following endoscopic findings: endoscopically estimated tumor size $\leq 2\text{cm}$, endoscopically mucosal cancer, and no ulcer in the tumor.

(evidence: moderate, recommendation: strong for)
Do you think total gastrectomy was necessary for a 45 years old lady with 1 cm signet ring cell carcinoma?

- Signet ring cell carcinoma, 1cm, limited in the lamina propria layer
What would you recommend for a 40 years old woman with a small flat signet ring cell carcinoma?
SRC. 10x6mm, lamina propria, clear resection margins, no lymphatic invasion
ESD for expanded indication

- ESD for expanded indication cases can be selectively performed in the individual cases.
- Flat small signet ring cell carcinomas are frequently treated by ESD in Korea.
Statement 2. Endoscopic resection could be performed for well or moderately differentiated tubular early gastric cancer or papillary early gastric cancers with the following endoscopic findings: endoscopically estimated tumor size >2 cm, endoscopically mucosal cancer, and no ulcer in the tumor or endoscopically estimated tumor size ≤3 cm, endoscopically mucosal cancer, and ulcer in the tumor. (evidence: moderate, recommendation: weak for)
Outcomes of ESD for EGC

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Outcome of endoscopic treatment of EGC with differentiated-type histology

1. ITT analysis (both curative and non-curative resection cases)
   - Comparison with surgery (propensity score matched cohort)

2. PP analysis
   1) Curative-resection cases: single-arm long-term data
   2) Non-curative resection cases: comparison between surgery group and observation group
Differentiated type EGC (2002-2012) (n = 3595)

Excluded:
1) LNM on CT or EUS (n = 6)
2) Previous gastric cancer (n = 20)
3) Cancer of other origin (n = 150)
4) Follow up < 2 years (n = 856)

EGC meeting indication treated with curative intent (n = 2563)

Endoscopic resection (n = 1290)

Surgery (n = 1273)

Propensity score matching

Endoscopic resection (n = 611)

Surgery (n = 611)

Pyo JH. Am J Gastroenterol 2016
Endoscopic resection surgery

Overall survival

Disease free survival

Disease specific survival

Recurrence free survival

Log rank P=0.827

Log rank P<0.001

Log rank P=0.891

Log rank P<0.001

Pyo JH. Am J Gastroenterol 2016
PP analysis (1): single-arm follow-up
- Differentiated, curative (n=1,306)

- EGCS treated by ESD at Samsung Medical Center
- 1,838 patients with 1,889 differentiated-type EGCS
- November 2003 – May 2011
- Censoring date: May 2014
- Differentiated-type EGC
  - Well or moderately differentiated or papillary EGC
  - According to the quantitatively predominant histologic type
  - Differentiated-type EGC > 50%
PP analysis (1): single-arm follow-up
- Differentiated, curative (n=1,306)

- Median follow-up: 61 months (range 17-122)
- **Local recurrence: 0.08% (1/1,306)**
- Metachronous recurrence: 3.6% (47/1,306)
  - Definition of metachronous recurrence: at least 12 months after ER
- **Extragastric recurrence: 0.15% (2/1,306)**
- 5-year overall survival
  - Absolute indication: 97.3%
  - Expanded indication: 96.4%
Overall-survival
- 1,306 curative ESDs from December 2003 to May 2011
Two extragastric recurrences (0.15%)
PP analysis (2): non-curative resection
- Comparison between surgery and observation group

Noncurative resection 341

Lateral margin positive 67 (19.6%)

Risk of lymph node metastasis 274 (80.4%)

Surgery 194 (70.8%)
- Lymph node 11 (5.6%)
- Local residual 10 (5.2%)

Observation 80 (29.2%)
- Patients’ refusal: 64
- High surgical risk: 8 (severe comorbidities)
- Concomitant advanced cancer in other organs: 8

Kim ER. Br J Surg 2015
Predictors of LN metastasis (5.7%)

Table 2: Comparison of clinicopathological characteristics according to the presence of lymph node metastasis among patients undergoing rescue surgery

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>No LN metastasis (n = 183)</th>
<th>LN metastasis (n = 11)</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>62.4 (8.4)</td>
<td>68.6 (8.7)</td>
<td>0.019†</td>
</tr>
<tr>
<td>Mean(s.d.)</td>
<td>63.0 (44–84)</td>
<td>68.1 (57–80)</td>
<td></td>
</tr>
<tr>
<td>Median (range)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sex ratio (M : F)</td>
<td>142 : 41</td>
<td>8 : 3</td>
<td>0.715</td>
</tr>
<tr>
<td>Tumour site</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antrum, angle</td>
<td>119 (65.0)</td>
<td>9 (82)</td>
<td>0.338</td>
</tr>
<tr>
<td>Body, fundus, cardia</td>
<td>64 (35.0)</td>
<td>2 (18)</td>
<td></td>
</tr>
<tr>
<td>Mean(s.d.) tumour size (cm)</td>
<td>2.1 (1.1)</td>
<td>2.6 (1.2)</td>
<td></td>
</tr>
<tr>
<td>Tumour depth</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mucosa</td>
<td>19 (10.4)</td>
<td>0 (0)</td>
<td>0.295‡</td>
</tr>
<tr>
<td>SM1</td>
<td>30 (16.4)</td>
<td>1 (9)</td>
<td></td>
</tr>
<tr>
<td>SM invasion depth ≥ 500 μm</td>
<td>134 (73.2)</td>
<td>10 (91)</td>
<td></td>
</tr>
<tr>
<td>Differentiation</td>
<td></td>
<td></td>
<td>0.128</td>
</tr>
<tr>
<td>Well differentiated</td>
<td>37 (20.2)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>Moderately differentiated</td>
<td>146 (79.8)</td>
<td>11 (100)</td>
<td></td>
</tr>
<tr>
<td>Lymphovascular invasion</td>
<td></td>
<td></td>
<td>1.000</td>
</tr>
<tr>
<td>No</td>
<td>76 (41.5)</td>
<td>5 (45)</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>107 (58.5)</td>
<td>6 (55)</td>
<td></td>
</tr>
</tbody>
</table>

Values in parentheses are percentages unless indicated otherwise. LN, lymph node; SM1, submucosal invasion depth less than 500 μm from muscularis mucosa layer; SM, submucosal. *χ² test, except †Student’s t test. ‡Mucosa or SM1 versus SM invasion depth of 500 μm or more.
Overall survival

- Median duration of follow-up after ER: 60.5 months (6-141)
Survival benefit of additional surgery
- Additional surgery: 127, follow-up: 67

Additional surgery group
Observation group
Is surgery necessary for mucosal cancer with lymphovascular invasion?

Table 3. Lymph node metastasis rate according to criteria in EGC patients with lymphovascular invasion

<table>
<thead>
<tr>
<th>Depth of invasion</th>
<th>Ulceration</th>
<th>Differentiated (%)</th>
<th>Undifferentiated (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mucosa</td>
<td>Ulcer (−)</td>
<td>≤ 2 cm</td>
<td>&gt; 2 cm</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0/28 (0)</td>
<td></td>
</tr>
<tr>
<td>Ulcer (+)</td>
<td>≤ 3 cm</td>
<td>3/24 (12.5)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1/2 (50.0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SM1</td>
<td>≤ 3 cm</td>
<td>7/61 (11.5)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>3/52 (5.8)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*SM1* < 500 μm from the muscularis mucosae
How to teach and learn ESD?

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Must knows before starting ESD

• Indications and skills for careful endoscopic evaluation for candidate lesions
• Advantages and disadvantages of each instrument
• Strategies for technically successful ESD
• How to manage complications

• Side by side hands-on training
H type ESD knife (Finemedix, Korea)
= Dual knife + IT-2 knife

Benign ulcer

EGC

W/D tubular adenocarcinoma 10mm in lamina propria, RM (-), L/V (-/-)
ONESTEP ESD knife (UPEX, Korea)

= Dual knife + injector
Most perforations can be treated endoscopically without surgery

- Primary closure of perforation

Tubular adenocarcinoma (M/D), in lamina propria, RM (-)
When the resection is big and close to the cardia or pylorus, short-term oral steroid can be used.

8 weeks later

6 months later
The hospital stay for gastric ESD is usually 4 days.
For the beginners, hands on training using a pig stomach model is very useful.
Side by side hands-on training
- Changing the role of the main operator and the first assistant
The first ESD of a young fellow endoscopist
Tele-mentoring using Facetime is a very useful tool for ESD beginners.

International mentoring is also possible. If you want some real-time comments from me, send me an e-mail (stomachlee@gmail.com).
Unforgettable case

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ESD for EGC in an surgical ICU
ESD for EGC in a patient on ECMO due to arrest by dilated cardiomyopathy
ESD for EGC in a patient on ECMO
- Tubular adenocarcinoma, M/D, 16x7mm, MM, L/V/N (-/-/-)
Take home message

• ESD is widely performed for EGCs in the absolute indication in Korea. Annually, its more than 7,000 cases.

• We are still very careful about expanded indication cases. It’s done usually for flat SRCs less than 1 cm.

• Starting the role of the first assistant is the beginning of learning ESD techniques.