Endoscopic Submucosal Dissection

Alessandro Repici MD
Professor of Gastroenterology
Director of Endoscopy
Director Fellowship Program
Humanitas University & Humanitas Research Hospital, Milano Italy
Disclosure

- Boston Scientific, consulting and advisory board
- Fujifilm Europe, consulting and research grant
- Ferring, research grant
- Cosmo Pharma, advisory board and consulting
- Norgine, consulting and research grant
- Takeda Russia, advisory board
In the history of gastrointestinal endoscopy, every once in a while a new therapeutic method comes to the fore that seems difficult and risky, yet so elegant and dramatic in its benefits and possibilities that it fires the desire of interventional endoscopists worldwide to perform it.

Charles J Lightdale, Editor  Gastrointest Endosc Clin N Am
EMR & Polypectomy – Size Limitations

Spiral/Serrated

Oval Braided

Small stiff thin wire
Piecemeal Resection

• Device-depending size of pieces

• Easy and fast

• Effective for most of the lesions to be resected

• Incomplete pathology
  • Lateral and vertical margins
  • Budding
  • Distance from tumor to resection margins
A new endoscopic mucosal resection procedure using an insulation-tipped electrosurgical knife for rectal flat lesions: report of two cases

Takuji Gotoda, MD, Hitoshi Kondo, MD, Hiroyuki Ono, Yutaka Saito, MD, Hajime Yamaguchi, MD, Daizo Saito, MD, Toshihiro Yokota, MD

First case in a 75-year-old man 20 mm flat rectal lesion (tubular adenoma) treated by using the IT knife and electrosurgical snare loop.
EMR with circumferential mucosal incision
Evolution to ESD

A successful single-step endoscopic resection of a 40 millimeter flat-elevated tumor in the rectum: endoscopic mucosal resection using sodium hyaluronate

Hironori Yamamoto, MD, Hirobumi Koiwai, MD, Tomizo Yube, MD, Norio Isoda, MD, Yukihiro Sato, MD, Yutaka Sekine, MD, Toshihiko Higashizawa, MD, Kenji Utsunomiya, MD, Kenichi Ido, MD, Kentaro Sugano, MD

GASTROINTESTINAL ENDOSCOPY, VOLUME 50, NO. 5, 1999

 Courtesy H. Yamamoto
Endoscopists have new challenges

- Mini-invasive resection of early superficial GI neoplasia
- Oncologically curative resection
- Precise T-staging of the disease
  - One-piece,
  - Clear tissue around,
  - Thick enough to have Sm
Free-hand – Surgical-like resection - ESD

- Endoscopist must use devices and techniques which deliberately allow them to define where and how deep to go with their cut
This Innovation came from Japan

• Japanese Masters have developed

  – Devices

  – Techniques

  – The specific pathology evaluation (m vs Sm1, ect)

  – The classification of the lesions/indication to ESD
What is required to perform ESD

• High volume center
• Advanced expertise in EMR
• Multidisciplinary team
• Dedicated equipment
  • Scopes
  • CO2
  • Distal attachments
  • Selection of devices
  • Proper solutions for submucosal elevation
3. Electrosurgical knives

1. Endoscope
2. Transparent hood
3. Electrosurgical knives
4. Hemostatic forceps
5. CO₂ gas insufflation

HF generator
Utility of Transparent Hood

- Better visualization of the operating field
- Give appropriate counter traction
What to inject in the submucosa?

- Hyaluronic acid
- Gelofusin
- Hyertonic solution
- Hydroxyethyl starch

Conclusions: There are several solutions in clinical use and many more under research, but most are poorly studied. SH seems to be clinically equivalent to NS. There are no significant differences in post-polypectomy complications. Larger RCTs are needed to determine any small differences that may exist between solutions.
Solution for elevation – FDA cleared - innovation

- Eleview
- Voluven 10%
- Gelafundin 4%
- Glycerol
- NaCl 0.9%

Repici A, et al, GIE submitted
Solution for elevation – FDA approved innovation

Eleview™

Sigmavisc® (sodium hyaluronate)
Which knife to be used

- IT knife
- Hook knife
- Hybrid-Knife
- TT knife
- Flush knife
- Dual knife
ESD – Western Barriers

- Technically demanding
- Labor intensive
- Time consuming
- Risk of complication
- Weak evidence on clinical relevance
ESD – The Clinical gain

• The idea of achieving an en bloc resection is both intriguing and rational

• The principal purpose of endoscopic treatment is to avoid surgery

• But how much evidence do we have to support this?
Indications according to Western Guideline

**Esophagus**
Squamous HGD/Ca
Barrett with large nodules or depressions

**Stomach**

**Colon - Rectum**
ESGE Guideline - Esophagus

**ESOPHAGUS**
Efficacy in the esophagus
Squamous cell cancer

ESGE recommends endoscopic en bloc resection for superficial esophageal squamous cell cancers (SCCs), excluding those with obvious submucosal involvement (strong recommendation, moderate quality evidence). Endoscopic mucosal resection (EMR) may be considered in such lesions when they are smaller than 10 mm if en bloc resection can be assured. However, ESGE recommends endoscopic submucosal dissection (ESD) as the first option, mainly to provide an en bloc resection with accurate pathology staging and to avoid missing important histological features (strong recommendation, moderate quality evidence).

**Barrett’s esophagus**

ESGE recommends endoscopic resection with a curative intent for visible lesions (strong recommendation, moderate quality evidence).

ESD has not been shown to be superior to EMR for excision of mucosal cancer, and for that reason EMR should be preferred. ESD may be considered in selected cases, such as lesions larger than 15 mm, poorly lifting tumors, and lesions at risk for submucosal invasion (strong recommendation, moderate quality evidence).

**SSC > 10 mm**  **En-bloc/ESD**
G2 adenoca, Sm1, < 500 micron, LV -, lateral and deep margin free of disease
G1 Barrett adenoca, Sm1, < 500 micron, G2 SSC m3, no LV invasion
What are the new findings?

- ESD and EMR are both highly effective for endoscopic eradication of early Barrett’s neoplasia. ESD has a higher technically complete resection rate but is more time consuming and severe adverse events can infrequently occur.

- In spite of initial technical advantages, ESD does not seem to offer clinical advantages over EMR in terms of need for surgery, neoplasia remission and early recurrence rates. Large volume randomised controlled trials would be required to verify significant differences with an adequate statistical power.
Overall R0 = 76%

EAC R0 = 56%

TABLE 3. Histopathology of ESD resected specimens

<table>
<thead>
<tr>
<th>Histopathologic findings</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>High-grade dysplasia, n (%)</td>
<td>14 (30.4)</td>
</tr>
<tr>
<td>Intramucosal adenocarcinoma, n (%)</td>
<td>17 (37)</td>
</tr>
<tr>
<td>EAC with at least submucosal involvement, n (%)</td>
<td>15 (32.6)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Degree of differentiation</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>G1 (well differentiated), n (%)</td>
<td>18 (56.2)</td>
</tr>
<tr>
<td>G2 (moderately differentiated), n (%)</td>
<td>10 (31.3)</td>
</tr>
<tr>
<td>G3 (poorly differentiated), n (%)</td>
<td>4 (12.5)</td>
</tr>
<tr>
<td>Presence of lymphovascular invasion, n (%)</td>
<td>9 (19.6)</td>
</tr>
</tbody>
</table>
Table 3: Technical outcomes of 142 completed ESD procedures according to centre

<table>
<thead>
<tr>
<th></th>
<th>Portsmouth</th>
<th>Milan</th>
<th>Zurich</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>No of procedures</strong></td>
<td>110</td>
<td>20</td>
<td>12</td>
<td>142</td>
</tr>
<tr>
<td><strong>En bloc resection, n/N (%)</strong></td>
<td>101 (91.8)</td>
<td>17 (85)</td>
<td>11 (91.7)</td>
<td>129 (90.8)</td>
</tr>
<tr>
<td><strong>R0 resection, n/N (%)</strong></td>
<td>85 (77.3)</td>
<td>18 (90)</td>
<td>9 (75)</td>
<td>112 (78.9)</td>
</tr>
<tr>
<td><strong>No of cancers resected</strong></td>
<td>91</td>
<td>15</td>
<td>11</td>
<td>117</td>
</tr>
<tr>
<td><strong>Curative resection for cancer (R0 resection of intramucosal and Sm1 cancer in the absence of poor prognostic features), n/N (%)</strong></td>
<td>61/91 (67)</td>
<td>11 (73.3)</td>
<td>5 (45.5)</td>
<td>77/117 (65.8)</td>
</tr>
</tbody>
</table>
ESD for Barrett

• Indication to be clarified (nodules/depression/Pattern)

• Low risk of complications

• Saving from surgery about half of patients with Ca

• Better evidence is needed to properly select patients suitable to ESD
Indications according to Western

- **Esophagus**: Squamous HGD/Ca Barrett with large nodules or depressions
- **Stomach**: EGC according to expanded Gotoda criteria
- **Colon - Rectum**
ESGE states that the majority of colonic and rectal superficial lesions can be effectively removed in a curative way by standard polypectomy and/or by EMR (strong recommendation, moderate quality evidence).

ESD can be considered for removal of colonic and rectal lesions with high suspicion of limited submucosal invasion that is based on two main criteria of depressed morphology and irregular or nongranular surface pattern, particularly if the lesions are larger than 20 mm; or ESD can be considered for colorectal lesions that otherwise cannot be optimally and radically removed by snare-based techniques (strong recommendation, moderate quality evidence).
Risk of submucosal invasion according to lesion morphology

Granular type H: 0%
Granular type M: 25%
Non-Granular type F: 33%
Non-Granular type PD: 65%

### Endoscopic predictors of deep mucosal invasion in colorectal LST

<table>
<thead>
<tr>
<th></th>
<th>Deep submucosal invasion(^1), n/N (%)</th>
<th>Univariate OR (95%CI)</th>
<th>Multivariate OR (95%CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>LST-G</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tumor size</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥4 cm</td>
<td>37/237 (16)</td>
<td>1.07 (0.62 – 1.85)</td>
<td></td>
</tr>
<tr>
<td>&lt;4 cm</td>
<td>26/177 (15)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tumor location</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right side</td>
<td>26/177 (15)</td>
<td>0.93 (0.54 – 1.60)</td>
<td></td>
</tr>
<tr>
<td>Left side</td>
<td>37/237 (16)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Large nodule</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥10 mm</td>
<td>55/316 (17)</td>
<td>2.37 (1.09 – 5.17)</td>
<td>11.7 (2.3 – 58.6)</td>
</tr>
<tr>
<td>&lt;10 mm</td>
<td>8/98 (8)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Depression</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Present</td>
<td>20/23 (87)</td>
<td>54.0 (15.4 – 189)</td>
<td>59.2 (9.0 – 387)</td>
</tr>
<tr>
<td>Absent</td>
<td>43/391 (11)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pit pattern: V(_1) (invasive)/V(_N)(^2)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Present</td>
<td>33/41 (80)</td>
<td>47.2 (20.0 – 111)</td>
<td>32.8 (12.2 – 87.8)</td>
</tr>
<tr>
<td>Absent</td>
<td>30/373 (8)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Histo: Sm1 adenocarcinoma, well differentiated, no LV invasion, lateral margins with features of adenocarcinoma
PRECISE EVALUATION OF LESIONS

• Predict advanced histology
  • Macroscopic appearance
  • Pit pattern
  • Vascular pattern
Low grade dysplasia (all blocks)
High grade dysplasia (one of 37 blocks)
Superficially Invasive carcinoma (pT1), one of 37 blocks

Block 20
width < mm 4, depth < mm 2, Ueno 2004
depth 540 micron, sm1
IBD lesions demand en-bloc resection
The potential impact of local excision for T1 colonic cancer in elderly and comorbid populations: a decision analysis

Andrew C. Currie, MRCS,1 Alan Askari, MRCS,1 Christopher Rao, PhD, MRCS,2 Brian P. Saunders, MD, FRCP,3,4 Thanos Athanasiou, MD, PhD,4 Omar D. Faiz, MS, FRCS,1,4 Robin H. Kennedy, MS, FRCS1,4

Harrow, London, United Kingdom
Colonic ESD

• Largest indications in Western Countries

• Lesion selection based on macro and pit pattern

• More technically demanding compared with gastric ESD

• Higher risk of complication

• Competitive to surgery for superficially invading lesions
A remarkable number of benign polyps are still referred to surgery

Adverse events after surgery for nonmalignant colon polyps are common and associated with increased length of stay and costs

Rajesh N. Keshani, MD,1 Ryan Law, DO,1 Jody D. Ciolino, PhD,2 Amy A. Lo, MD,3 Adam B. Gluskin, MD,1 David J. Bentrem, MD,4 Sri Komanduri, MD,1 Jennifer A. Pacheco, BA,2 David Grande, BS,1 William K. Thompson, PhD2

Colectomy for Endoscopically Unresectable Polyps: How Often Is It Cancer?
AEs associated to surgery are higher than colorectal ESD

Benign Polyps deemed unresectable by endoscopy

<table>
<thead>
<tr>
<th>Journal</th>
<th>N° of patients</th>
<th>% benign</th>
<th>AEs%</th>
<th>LOS (days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dis Col Rectum 2012</td>
<td>750</td>
<td>83.3</td>
<td>9.8</td>
<td>NA</td>
</tr>
<tr>
<td>GIE 2016</td>
<td>359</td>
<td>90</td>
<td>17.7</td>
<td>5.2</td>
</tr>
<tr>
<td>Surg Endosc 2016</td>
<td>34</td>
<td>82</td>
<td>18</td>
<td>3.8</td>
</tr>
<tr>
<td>Surg Endosc 2008</td>
<td>63</td>
<td>80</td>
<td>12</td>
<td>NA</td>
</tr>
<tr>
<td>Int J Colorect Dis 2009</td>
<td>58</td>
<td>100</td>
<td>9.3</td>
<td>4.9</td>
</tr>
</tbody>
</table>
Buon Natale to all!