ENDOSCOPY IN GASTRIC CANCER: NEW IMAGING TECHNIQUES, NEW TREATMENT MODALITIES (EMR, ESD)

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October the 6th 2017,
No conflict of interest to declare
In these studies EUS does not have therapeutic impact on the decision to perform chemotherapy, but most of team began to perform EUS for gastric ECA staging.
## EUS STAGING

<table>
<thead>
<tr>
<th></th>
<th>T1+T2 VS T3-T4</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sensitivity</strong></td>
<td>86%</td>
</tr>
<tr>
<td><strong>Specificity</strong></td>
<td>91%</td>
</tr>
<tr>
<td><strong>PPV</strong></td>
<td>98%</td>
</tr>
<tr>
<td><strong>NPV</strong></td>
<td>65%</td>
</tr>
<tr>
<td><strong>Accuracy</strong></td>
<td>89%</td>
</tr>
</tbody>
</table>

**meta-analysis, 54 studies, 5601 patients**

Mocelli et al, GIE 2011
LYMPH NODE INVASION AND EUS

- Sensitivity = 83%
- Specificity = 67%
- Heterogeneity of studies needs to consider carefully results of EUS

- Metanalysis of 44 studies

Mocellin S, Pasquali S. Diagnostic accuracy of endoscopic ultrasonography (EUS) for the preoperative locoregional staging of primary gastric cancer. Cochrane Database, 2015
• N staging with EUS>TDM staging-77/71% for gastroesophageal junction (1)

• But regional lymph nodes impact the therapeutic only for T1N0 which has not neo-adjuvant chemotherapy. Controversy exists with T2N0 because 20-30% of these are T1N0

2) Kleimberg L, Brock M, Gibson M. Management of locally advanced adenocarcinoma of the esophagus and gastroesophageal junction: finally a consensus. Curt Treat Options Oncol 2015
EUS STAGING: RELIABILITY OF BIOPSY

Needle tract seeding: only 3 cases reported. Exceptional.

Lymph nodes: Specificity for adenocarcinoma is considered around of 100%. Sensitivity varies from 87 to 100%. Only one study with pathological findings found sensitivity of 83% and specificity of only 93% for oesophageal cancer.

EUS staging

TNM 2010

French thesaurus
EUS STAGING: DISTANT LESIONS

EUS-FNA can change therapeutic management in 8-23%

Mortensen et al: Prospective study of 62 patients. Therapeutic changed in 8% of the patients after exclusion of suspected metastasis lesions on CT-scan

Hassan et al: retrospective study of 234 patients. Therapeutic management changed in 15% of the patients

Araujo et al: Retrospective study of 115 patients. Therapeutic management changes in 23% of the patients

Metastases of left liver lobe was diagnosed in 3-5% of the patients for esophageal cancer with 100% specificity.


In patient with gastric cancer, the main utility of EUS-guided sampling is to avoid unnecessary surgery, demonstrating distant lymph nodes or other lesions indicating the patient for palliation (ESMO-ESSO-ESTRO).

In gastric cancer, ESGE recommends against EUS-guided sampling of local LNs and suggest EUS-guided sampling of distant LNS, or other distant lesions (metastases) if it may impact treatment decisions.


Dumonceau JM, Deprez PH, Jenssen C et al. Indications, results, and clinical impact of endoscopic ultrasound (EUS)-guided sampling in gastroenterology: European society of gastrointestinal endoscopy (ESGE) clinical guideline-Updated January 2017
EUS staging is more reliable than others techniques.

EUS staging will not change therapeutic management. Neo-adjuvant chemotherapy is already decided.

**EUS staging**, looking for **distant lesions** will change your therapeutic management in 8 to 23% finding lesion which will change the status of the patient (local disease to metastatic disease)

**EUS staging needs biopsies.** But we cannot biopsy all suspicious lymph nodes.
How to improve the LN Staging?

Sonovue

ELASTOSONOGRAPHY

Distortion

Colorisation

Hard

Soft

FNA

nCLE
CONTRAST ENHANCEMENT

Carcinoma: heterogenous enhancement, focal cortical thickening, focal contrast enhancement

lymphoma: variable contrast enhancement, intense homogeneous enhancement most of time

inflammatory lymph nodes: centrifugal and homogenous pattern

Cui XW, Jenssen C Saftoiu A et al. New ultrasound techniques for lymph node evaluation. WJG, 2013
RATIO-ELASTOGRAPHY
MULTICENTRE PROSPECTIVE STUDY ON EUS ELASTOGRAPHY. Giovannini et al: WJG, 2009
EUS ELASTOGRAPHY

METANALYSIS:

EUS elastography & LN *

Differentiation Benign vs Malignant

368 Pts including 431 LN

Pooled Sensitivity = 88%

Pooled Specificity = 85%

*Xu W. et al : GIE, 2011, 74(5), 1001-9*
An essential limitation of lymph nodes evaluation is the lack of benchmark histology in most of the studies. Only surgical piece can be a real gold standard for pathology.

In the study lead by Mortensen et al, a reliable benchmark histology decreases in the final results sensitivity and specificity.

We probably have to be cautious in the diagnosis of benign/malignancy for lymph nodes given by literature data.

sensitivity = 55%
specificity = 82%

31% of the patients are excluded in this study.

TRYING TO IMPROVE ACCURACY OF LN-STAGING

- AQ-flex probe
- 19G needle

Endomicroscopy, CLE

Caillol et al, UEGW 2012
TRYING TO IMPROVE ACCURACY OF LN-STAGING

NORMAL LYMPH NODE

Reticular pattern
Lymphocytes
METASTASIS GASTRIC ADENOCARCINOMA

Irregular distribution of cells with fibers

Irregular distribution of cells

Glands
FIDUCIAL MARKERS: AN HELP FOR RADIATION THERAPY

- Gold markers of 3mm
- inserted under EUS and X-ray
- Size of the needle: 22G

Caillol et al, UEGW 2016
FIDUCIAL MARKERS: AN HELP FOR RADIATION THERAPY

Caillol et al, UEGW 2016
• **Fiducor study:**

  - The GTV changed significantly in **89%** of the cases (13/15)
  - One (7%) patient had a distant lymph node metastasis in oesophagus cancer not seen with CT-scan.

Caillol et al, UEGW 2016
GASTRIC CANCER

scanner

TUMOR M0

- Distant LN
- Mediastinum,
- Aortico-caval
- liver metastasis
- carcinosis
- Biopsy+++++

EUS

T1N0

CHEMOTHERAPY

T 2-3/N0-1

SURGERY + NEOADJUVANT CT

SURGERY
An endoscopic treatment is a local treatment for lesion without lymph nodes metastasis.
ENDOSCOPIC TREATMENT: ESD/EMR

ESD technique

EMR technique

image from medscape

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>EMR Events</th>
<th>EMR Total</th>
<th>ESD Events</th>
<th>ESD Total</th>
<th>Risk Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Events</td>
<td>Total</td>
<td>Events</td>
<td>Total</td>
<td>M-H Random. 95% CI</td>
</tr>
<tr>
<td>Oka, 2006</td>
<td>95</td>
<td>825</td>
<td>26.5%</td>
<td>2.49 [1.86, 3.34]</td>
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</tr>
<tr>
<td>Oda, 2006</td>
<td>112</td>
<td>102</td>
<td>125</td>
<td>0.45 [0.02, 1.16]</td>
<td></td>
</tr>
<tr>
<td>Watanabe, 2006</td>
<td>3</td>
<td>42</td>
<td>8.8%</td>
<td>0.10 [0.05, 0.20]</td>
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</tr>
<tr>
<td>Yokoi, 2006</td>
<td>40</td>
<td>182</td>
<td>Not estimable</td>
<td>Not estimable</td>
<td></td>
</tr>
<tr>
<td>Chol, 2006</td>
<td>7</td>
<td>46</td>
<td>15.0%</td>
<td>0.80 [0.53, 1.21]</td>
<td></td>
</tr>
<tr>
<td>Shimura, 2007</td>
<td>10</td>
<td>61</td>
<td>12.9%</td>
<td>0.18 [0.07, 0.44]</td>
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</tr>
<tr>
<td>Hiratsuka, 2008</td>
<td>1</td>
<td>13</td>
<td>4.2%</td>
<td>2.00 [0.71, 5.62]</td>
<td></td>
</tr>
<tr>
<td>Catalano, 2009</td>
<td>3</td>
<td>12</td>
<td>2.3%</td>
<td>2.80 [0.60, 13.35]</td>
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<tr>
<td>Hoteya, 2009</td>
<td>17</td>
<td>17</td>
<td>9.9%</td>
<td>0.94 [0.53, 1.67]</td>
<td></td>
</tr>
<tr>
<td>Min, 2009</td>
<td>3</td>
<td>6</td>
<td>55.5%</td>
<td>0.98 [0.18, 5.37]</td>
<td></td>
</tr>
<tr>
<td>Nakamoto, 2009</td>
<td>4</td>
<td>22</td>
<td>18.2%</td>
<td>1.38 [0.46, 4.12]</td>
<td></td>
</tr>
<tr>
<td>Hoteya, 2010</td>
<td>8</td>
<td>22</td>
<td>37.5%</td>
<td>1.10 [0.11, 11.46]</td>
<td></td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>1762</td>
<td>2044</td>
<td>100.0%</td>
<td>1.22 [0.76, 1.97]</td>
<td></td>
</tr>
<tr>
<td>Total events</td>
<td>136</td>
<td>136</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heterogeneity:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tau^2:</td>
<td>0.21</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chi^2:</td>
<td>17.27</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>df:</td>
<td>9</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>P (M-H Random.):</td>
<td>0.04</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I^2:</td>
<td>48%</td>
<td></td>
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</tbody>
</table>

**Fig. 6** Bleeding risk for endoscopic submucosal dissection (ESD) versus endoscopic mucosal resection (EMR) for early gastric cancer

**Fig. 7** Perforation rates for endoscopic submucosal dissection (ESD) versus endoscopic mucosal resection (EMR) for primary and recurrent early gastric cancer
**EMR/ESD: DURATION OF THE PROCEDURE**

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>ESD</th>
<th>EMR</th>
<th>Std. Mean Difference</th>
<th>IV, Random, 95% CI</th>
<th>Std. Mean Difference</th>
<th>IV, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td>742</td>
<td>1111</td>
<td>100.0%</td>
<td>1.55 [0.74, 2.37]</td>
<td>1.55 [0.74, 2.37]</td>
<td></td>
</tr>
</tbody>
</table>

Fig. 8 Resection time of endoscopic submucosal dissection (ESD) versus endoscopic mucosal resection (EMR) for primary and recurrent early gastric cancer

EMR/ESD: COMPLETE RESECTION RATE


<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>ESD</th>
<th>EMR</th>
<th>Risk Ratio</th>
<th>Risk Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Events</td>
<td>Total</td>
<td>Events</td>
<td>Total</td>
</tr>
<tr>
<td>4.1.1 &lt; 1 year</td>
<td>0</td>
<td>572</td>
<td>13</td>
<td>326</td>
</tr>
<tr>
<td>Hoteya, 2009</td>
<td>0</td>
<td>572</td>
<td>13</td>
<td>326</td>
</tr>
<tr>
<td>Min, 2009</td>
<td>9</td>
<td>243</td>
<td>0</td>
<td>103</td>
</tr>
<tr>
<td>Hoteya, 2010</td>
<td>0</td>
<td>40</td>
<td>2</td>
<td>22</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>9</td>
<td>15</td>
<td>15</td>
<td>15</td>
</tr>
<tr>
<td>Total events</td>
<td>4</td>
<td>63</td>
<td>63</td>
<td>63</td>
</tr>
<tr>
<td>Heterogeneity:</td>
<td>Tau² = 7.56; Chi² = 9.00, df = 2 (P = 0.01); I² = 78%</td>
<td>Test for overall effect: Z = 0.73 (P = 0.47)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Fig. 5** Local recurrence rates for endoscopic submucosal dissection (ESD) versus endoscopic mucosal resection (EMR) for early gastric cancer according to follow-up period
ENDOSCOPIC TREATMENT: EVALUATION BEFORE RESECTION
Videoendoscopy exploration is mandatory. Risk of metachronous lesions exists. The cumulative 3-years risk is 5.9%.

EUS is not always mandatory

<table>
<thead>
<tr>
<th></th>
<th>Nb Patients</th>
<th>EUS Accuracy</th>
<th>Endoscopy Acc.</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Choi,2010 *</td>
<td>388</td>
<td>78,9%</td>
<td>81,4%</td>
<td>0,052</td>
</tr>
<tr>
<td>Song, 2010</td>
<td>955</td>
<td>67,4%</td>
<td>73,7%</td>
<td>&lt;0,001</td>
</tr>
</tbody>
</table>

• ESGE suggests that a strategy of precise endoscopic evaluation of these lesions is sufficient for predicting resectability, with EUS reserved only for selected cases.

ESGE recommends endoscopic resection for the treatment of gastric superficial neoplastic lesions that possess a very low risk of lymph node metastasis (strong recommendation, high quality evidence). EMR is an acceptable option for lesions smaller than 10–15 mm with a very low probability of advanced histology (Paris 0-IIa). However, ESGE recommends ESD as treatment of choice for most gastric superficial neoplastic lesions (strong recommendation, moderate quality evidence).

ENDOSCOPIC FINDINGS: JAPANESE CLASSIFICATION

**TYPE I**

**TYPE III**

- 90-95% SM +

**TYPE II**

- IIA
- IIB
- IIC

- 80-85% IE
Resecting the correct lesion

Diagnose

Evaluation: IIc

Resection
JAPANESE GUIDELINE

- Indication for endotherapy: Expanded Criteria

  - Macroscopically intramucosal (cT1a) differentiated carcinomas measuring less than 2cm

- UL-, differentiated carcinomas > 2cm, LV- 

- UL+, differentiated carcinomas < 3cm, LV- 

- UL-, undifferentiated carcinomas < 2cm, LV-

• Lymph nodes metastatic risk is for expanded criteria is 0.4% (2678 patients)

Choi KK, Bae JM, Kim SM et al. The risk of lymph node metastases in 3951 surgically resected mucosal gastric cancers: implications for endoscopic resection. GIE 2016;83(5):896-901

LONG TERM FOLLOW-UP AFTER CURATIVE RESECTION WITH EXPANDED CRITERIA

1537 patients from 1999 to 2010
curative resection with expanded criteria
mean follow-up= 83.3 months
80 patients without follow-up

8 patients with relapse (0.5%)

242 patients with curative resection for metachronous lesions: no death cancer related to these metachronous lesions

Size in expanded criteria: Superficial carcinoma, follow-up

size out of expanded criteria: time of resection: 6h
Histopathology: Sm3
LONG-TERM FOLLOW-UP AFTER NON CURATIVE ESD FOR EGC:

IS ESD WITHOUT CURATIVE TREATMENT A BAD PREDICTOR FACTOR FOR THE DISEASE OF THE PATIENT?

569 patients from 1999 to 2010
Patients with potential risk of metastatic lymph nodes

5-years DSS (Disease Specific Survival) was 98.8% after gastrectomy

Lymph nodes metastasis found in 5% of the cases

Suzuki H, Oda I, Abe S et al Clinical outcomes of early gastric cancer patients after non curative endoscopic submucosal dissection in a large consecutive patient series. Gastric Cancer 2017
# Metachronous Lesions: An Impact on the Surveillance

<table>
<thead>
<tr>
<th></th>
<th>5-year</th>
<th>7-year</th>
<th>10-year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cumulative incidence of MGC</td>
<td>10%</td>
<td>13%</td>
<td>23%</td>
</tr>
</tbody>
</table>

1526 ESD included in follow-up

Screening

・「Gastric cancer patients who had gastroscopy performed within 5-years before cancer diagnosis have significantly lower mortality. Our results may support the role of repeat endoscopic examination or surveillance endoscopy in selected patients.」

Only less than 10% of gastric carcinoma are EGC (early gastric cancer) in western countries/ 60% in Eastern countries.

10% of EGC are misdiagnosed as gastritis, erosion or ulcers.

With experienced endoscopist the diagnosis of EGC in patients referred for dyspepsia can increase from 1% to 26% in an united kingdom registry.

As a result, video-endoscopy with high definition is also a new imaging in the management of gastric cancer. Detection of EGC will improve the survival rate of this cancer.

CONCLUSION

- EUS is essential to detect distant lymph nodes, carcinosis, left lobe liver metastasis and these lesions need to be punctured. T staging with EUS can be discussed.

- Endoscopic resection is the first line therapy for early gastric tumours. Strict criteria of resection have to be applied.
GASTRIC CANCER

Endoscopic aspect

Scanner

TUMOR M0

- Distant LN
- Mediastinum, Aortico-caval
- liver metastasis
- carcinomes
- Biopsy+++++

Endoscopic aspect

T1N0

CHEMOTHERAPY

EUS

Surgery +
NEOADJUVANT CT

T 2-3/N0-1

Neoadjuvant chemotherapy?

SURGERY