Looking better at the esophagus: early detection of Squamous Cell Cancer and Adenocarcinoma

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Head of Endoscopy

SQUAMOUS ESOPHAGEAL CANCER
Daily Challenges in Digestive Endoscopy for Endoscopists and Endoscopy Nurses
BSGIE Annual Meeting
18/09 2014- Mechelen

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Lugol 1-3 % solution normal non keratinised glycogen containing squamous mucosa stains dark - glycogen layer
Unstained area’s: Barrett, inflammation, dysplasia, SCC

Look better in patients at risk!

- ENT tumors
- Lung tumors
- Achalasia
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CHROMO-ENDOSCOPY

- Indications Lugol:
  - screening for squamous cancer in high risk patients

326 Patients with Head and Neck cancer
Standard WL endoscopy → Lugol 2%

Esophageal neoplasia: 7.36%
WL and Lugol same accuracy for advanced and invasive cancer
HGIN: 55% detected by WL ↔ 100% Lugol 2%

Hashimoto CL et al, AJG 2005 100: 275

1095 Patients with history of
1) Head and Neck cancer or Lung Cancer
2) Alcoholic pancreatitis
3) Alcoholic cirrhosis
4) Alcohol or tobacco addiction
NO esophageal symptoms

Esophageal neoplasia: 3.2%
20% of cancer only detected after lugol staining
HGIN: 66% only detected after lugol staining

Group 1: cancer + dysplasia: 9.9%

Dubuc et al, Endoscopy 2006 38 690

NBI in high risk patients for SCC

350 High risk patients
Current or present Head and Neck cancer or Lung Cancer
Current or past SCC

Experienced endoscopist
> 9 years as endoscopist
2 year NBI experience
SENSITIVITY 100%

Less Experienced endoscopist
3-5 years as endoscopist and experience with lugol
NBI observation for 2-3 months
SENSITIVITY 53%


CONCEPT OF PAN-UPPER-ENDOSCOPY

Upper GI ENDOSCOPY + Lugol

• ENT Tumors
• Lung cancer
• Squamous esophageal cancer

Bronchoscopy
Laryngoscopy
Achalasia is a risk factor for SCC, but despite endoscopic surveillance, cancer is diagnosed at an advanced stage. Efforts should be made to identify high risk groups and develop adequate surveillance strategies.

Leeuwenburgh et al AM J Gastro 2010; 105::2144-2149

1/43 patients with carcinoma in situ, all detected with WL, NBI and lugol


Achalasia Cohort of 448 achalasia patients Median 9.6 years follow-up
3.3% developed cancer 0.34 % risk / year
10/15 advanced stage 5 esophageal resection

Meta-analysis NBI and Barrett

Inclusion criteria
- Prospective clinical studies and randomized controlled trials;
- published in peer-reviewed journals;
- assessment of dysplasia and/or noninvasive EAC as one of their outcomes;
- included both WLE with RB and CE (or VC) with targeted biopsies;
- extractable information regarding the diagnostic yield of WLE vs CE (or VC).

14 studies with MB or IC CE/ NBI

1. advanced imaging techniques increased the diagnostic yield for detection of dysplasia or cancer by 34%
2. Virtual chromoendoscopy significantly increased the diagnostic yield by 34% and chromoendoscopy by 35%
3. There was no significant difference between virtual chromoendoscopy and chromoendoscopy.

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### ZOOM NBI in Barrett

Meta-analysis of 8 studies on Zoom NBI
8 studies were selected
\[ N = 446 \text{ patients / 2194 lesions (sites)} \]

<table>
<thead>
<tr>
<th></th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Odds ratio</th>
<th>AUC</th>
</tr>
</thead>
<tbody>
<tr>
<td>HGIN</td>
<td>0.96</td>
<td>0.94</td>
<td>342.49</td>
<td>0.99</td>
</tr>
<tr>
<td>SIM</td>
<td>0.95</td>
<td>0.65</td>
<td>37.53</td>
<td>0.88</td>
</tr>
</tbody>
</table>

"NBI with magnification is accurate with high diagnostic precision for diagnosis of HGD in Barrett's esophagus on the basis of irregular mucosal pit patterns and/or irregular microvasculature."

Mannath J et al Endoscopy 2010;42:351

### Pay attention when reading BE papers

1. Detection ≠ Characterization
2. Experts ≠ Beginners
3. Studies ≠ General practice

### New NBI data: is this useful in clinical practice

- Multicenter cross over trial HDWL and NBI
  - Three expert referral centers
  - 48% dysplasia in 123 patients

P. Sharma et al Gut 2013
New NBI data: is this useful in clinical practice

• What are the new findings?
  – When compared with high-definition white light endoscopy, NBI detected the same number of patients with intestinal metaplasia but with fewer biopsies.
  – NBI detected a higher proportion of areas with dysplasia.
  – Regular appearing NBI surface patterns did not harbor high-grade dysplasia/cancer.
  – The accuracy of NBI for the detection of low grade dysplasia is low.

P. Sharma et al Gut 2013

New NBI data: is this useful in clinical practice

• Result section of the paper
  – NS difference for detected visible lesions with neoplasia but HDWL (17.1%) detected more patients with visible lesions than NBI (4.9%)!
  – NS difference for number of patients with dysplasia
  – NBI did not detect more patients with higher grades of dysplasia according to the targeted biopsies

P. Sharma et al Gut 2013

CONCLUSION SHOULD BE: IF YOU ARE NOT AN EXPERT IN ADVANCED IMAGING AND DETECTING EARLY CANCER: USE HD WL AND TAKE PROPER BIOPSIES

New NBI data: is this useful in clinical practice

• Result section of the paper
  – The conclusion is based on the area based analysis showing a difference in proportion of lesions with any dysplasia (LGIN/HGIN/EAC)
    – 67/321 HDWL (21%) vs 81/267 (30%) (p=0.01)

P. Sharma et al Gut 2013

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**Meta-analysis NBI and Barrett**

Meta-analysis of the effects of endoscopy with narrow band imaging in detecting dysplasia in Barrett’s esophagus

J. Song, J. Zhang, J. Wang, X. Cen, Y. Yu, J. Wang, Y. Liu, W. Dong
Department of Gastroenterology, Renmin Hospital of Wuhan University, Wuhan, Hubei, China

Inclusion criteria
- Prospective trial
- Histology gold standard
- Description of vascular and pit pattern

<table>
<thead>
<tr>
<th></th>
<th>Sensitivity SIM</th>
<th>Specificity SIM</th>
<th>Sensitivity HGD</th>
<th>Specificity HGD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Per patient</td>
<td>0.91</td>
<td>0.85</td>
<td>0.91</td>
<td>0.95</td>
</tr>
<tr>
<td>Per lesion</td>
<td>0.97</td>
<td>0.64</td>
<td>0.69</td>
<td>0.90</td>
</tr>
</tbody>
</table>

7 studies included

Song et al Dis Eso 2014 online

**NBI in Barrett’s Esophagus**

NBI Characterization of Barrett’s epithelium

Simplified system

Type A: columnar glands without IM
(round pits with regular microvasculature)

Singh et al Endoscopy 2008

Type B: columnar glands with IM
(villus / ridge pits with regular microvasculature)
Singh et al Endoscopy 2008

Type C: columnar glands with IM
(absent pits with regular microvasculature)
Singh et al Endoscopy 2008
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NBI in Barrett’s Esophagus

NBI Characterization of Barrett’s epithelium

Simplified system

Type D: high grade dysplasia

distorted pits with irregular microvasculature

Singh et al Endoscopy 2008

NBI Characterization of Barrett’s epithelium

Diagnostic Accuracy of a simplified system

<table>
<thead>
<tr>
<th></th>
<th>PPV</th>
<th>NPV</th>
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<tbody>
<tr>
<td>Type A</td>
<td>100%</td>
<td>97%</td>
</tr>
<tr>
<td>Type B+C</td>
<td>88%</td>
<td>91%</td>
</tr>
<tr>
<td>Type D</td>
<td>81%</td>
<td>99%</td>
</tr>
</tbody>
</table>

Singh et al Endoscopy 2008

Diagnostic Accuracy of a simplified system

<table>
<thead>
<tr>
<th></th>
<th>sens</th>
<th>Spec</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dyspl : LGIN-CA</td>
<td>49%</td>
<td>73%</td>
</tr>
<tr>
<td>Dyspl : HGIN+CA</td>
<td>63%</td>
<td>66%</td>
</tr>
</tbody>
</table>

Singh et al Endoscopy 2011; 43: 745–751

252 NBI images of 75 patients

3 experts

4 non-experts

Fig. 1 Relationship between current and simplified classification of narrow band imaging (NBI) surface patterns for predicting Barrett’s esophagus histology.

Singh et al Endoscopy 2011; 43: 745–751

"the interobserver agreement was fair with suboptimal sensitivity and specificity. Significant improvements in NBI interpretation are needed prior to the routine use of NBI surface patterns for the assessment of Barrett’s esophagus”

Singh et al Endoscopy 2011; 43: 745–751
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NBI for BE detection and characterisation

• NBI has good accuracy in individual studies (pooled in a meta-analysis).
• However interobserver agreement is only fair …..
• Can this be used in a non-expert setting?

Advanced imaging and Barrett: selection Bias

<table>
<thead>
<tr>
<th>ref</th>
<th>n</th>
<th>modality</th>
<th>prevalence</th>
</tr>
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<tbody>
<tr>
<td>Kara M 2006</td>
<td>63</td>
<td>NBI zoom</td>
<td>58%</td>
</tr>
<tr>
<td>Kara M 2006</td>
<td>20</td>
<td>AFI+ NBI zoom</td>
<td>70%</td>
</tr>
<tr>
<td>Sharma 2006</td>
<td>51</td>
<td>NBI zoom</td>
<td>14%</td>
</tr>
<tr>
<td>Curvers 2008</td>
<td>84</td>
<td>AFI+ NBI zoom</td>
<td>36%</td>
</tr>
<tr>
<td>Singh 2008</td>
<td>109</td>
<td>NBI zoom</td>
<td>13%</td>
</tr>
<tr>
<td>Goda 2007</td>
<td>36</td>
<td>NBI zoom</td>
<td>11%</td>
</tr>
<tr>
<td>Anagnostopoulos 2008</td>
<td>50</td>
<td>NBI zoom</td>
<td>20%</td>
</tr>
<tr>
<td>Hamamoto 2004</td>
<td>11</td>
<td>NBI zoom</td>
<td>0%</td>
</tr>
<tr>
<td>Wolfsen 2007</td>
<td>65</td>
<td>NBI</td>
<td>57%</td>
</tr>
<tr>
<td>Sharma et al 2013</td>
<td>123</td>
<td>NBI</td>
<td>14%</td>
</tr>
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</table>

Most study populations

The real challenge
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The real challenge

Inspect better!

Inspect better!

Gupta et al, Gastrointest Endosc 2012

Gupta et al, Gastrointest Endosc 2012
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HD-endoscopy

Loss of aceto whitening

132 patients (61% surveillance)
Acetic acid 2.5%

Cut off 142 seconds
Sensitivity 98%
Specificity 84%
For neoplasia

14.7 fold increase in detection in comparison to random biopsies

Longcroft-Wheaton et al Endoscopy 2013 45: 426–432
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Use your best available endoscope

Barrett screening

Fiberoptic
Standard high resolution endoscope
High definition endoscope

Pech et al Endoscopy 2007; 39: 588±593
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Accidental finding of Barrett on reflux screening
Barrett screening program
Follow-up of HGIN or LGIN in Barrett

Use best endoscope
First look than biopsy
AGA guidelines :
2 endoscopies with 1 year interval no dysplasia → 3 year interval
Seattle protocol : 4 Q biopsies every 2 cm
CURRENTLY NO ROLE FOR SYSTEMATIC ADVANCED IMAGING

Wang et al AM J Gastro 2008;103:788
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Conclusions: SCC

- Squamous cell cancer
  - Look better in patients at risk
  - Pinkish areas resembling Barrett should raise suspicion
  - USE LUGOL in patients with
    - ENT cancer
    - Lung Cancer
    - Long standing achalasia

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**Conclusions : Barrett**

- Advanced imaging increases the diagnostic yield in experienced hands for patients referred for suspicion of neoplasia.
- There is currently insufficient data to abandon the classical Seattle protocol.
- Further studies are needed to assess how detection can be improved in:
  - General secondary care units
  - Low risk surveillance population

**Conclusions : Barrett**

- Look first well and long enough
  - Clean the esophagus
  - Retroflex
  - HD endoscopes
- Start using advanced imaging techniques to increase your diagnostic yield
- Finish with a classical Seattle protocol.