Managing dysplasia in Barrett’s Oesophagus

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Barrett’s oesophagus
pre-malignant condition

Vienna classification
- Category 1: Negative for dysplasia
- Category 2: Indefinite for dysplasia
- Category 3: Low grade dysplasia
- Category 4: High grade dysplasia
- Category 5: Invasive neoplasia
  > Intramucosal carcinoma
  > Sub-mucosal invasive carcinoma


Barrett’s with Dysplasia / early neoplasia

Detect → Characterize → Treat

Barrett’s with Dysplasia / early neoplasia

High grade “Intramucosal cancer” sm1 sm2 sm3

0% 0-4% 1-12% 26% 44%

Risk of nodal metastases

Westerterp M et al. Virchows Arch 2005;446:497
Catalano MF et al. Gastrointest Endosc 1996;87:1245

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Gastrointestinal Endosc 2003;58(6):S3-S43
Rationale for Endoscopic therapy

- Even in expert centers the operative mortality is 3-5% and morbidity 40-50%.
- Risk of lymph node metastases is negligible (less than 30 day mortality of oesophagectomy).
- Negative impact on QOL (at least for the first 1-2 yrs).
- Not all patients are fit for major surgery.
- Newer attractive treatment options with promising results.

Work-up for patients with Dysplasia / early Ca.

1. Endoscopic / Radiology imaging
2. Histo-pathological evaluation
3. Accurate staging of the lesions

HD endoscopy

Acetic acid enhanced endoscopy

Endoscopic Trimodal Imaging (ETMI)

- High Resolution Magnification Endoscopy (HRME)
- Autofluorescence Imaging (AFI)
- Narrow Band Imaging (NBI)

HR- Endoscopy Vs HR-EUS prediction of T stage in Barrett’s early neoplasia

- HR Endoscopic diagnosis based on Paris classification (0-IIa, 0-IIb, 0-IIc)
- HR EUS with 20Mhz mini-probe
- Overall accuracy 80%, no difference between HR-E & HR-EUS
Submucosal invasion is detected by EUS for 26% of patients with early Barrett’s neoplasia. The value of EUS staging before resection for type 0-IIb early Barrett’s cancer (flat lesions) is limited because 100% of these lesions are limited to the mucosa. For the management algorithm in this selected cohort, the use of EUS should be reconsidered.

Role of EUS: to R/O advanced stage

- T staging accuracy ~ 75%
- N staging accuracy 90% (with FNA)
- High NPV (>95%) to R/O LN & deep invasion

What endoscopic therapies are available?

- Argon Plasma Coagulation
- Laser ablation (Nd-Yag, Diode, KTP etc.)
- Multi-polar electro-coagulation (MPEC).
- Photodynamic therapy
- Radiofrequency ablation
- Cryospray therapy
- Endoscopic Mucosal Resection

Photodynamic therapy

- 102 patients randomized to PDT Vs omeprazole
- HGD eradication 77% Vs 39%
- 5 years follow-up (61 patients only)
- PDT better than omeprazole in preventing cancer (15% Vs 29%)

Overholt BF et al. Gastrointest Endosc 2007;66:460-468

Argon Plasma Coagulation

- 29 patients with Barrett’s with HGD
- Unfit or declined surgery
- Follow-up over 7 years (mean 37 months)
- 86% eradication
- 1 perforation, no strictures

Attwood SE et al Clin Gastroenterol/Hepatol 2003;1:258-263

Ablation of dysplastic Barrett’s oesophagus: PDT Vs APC

- APC and PDT are comparable in the mucosal ablation of dysplastic Barrett’s oesophagus
- PDT is three times more expensive than APC

Ragunath K et al. Gastroenterol Endosc 2005;47:750-756

APC Vs MPEC

- 35 patients, 2 yrs follow-up
- ~ 70% response irrespective of technique
- 1 stricture, no major complications


Draw backs with ablation technique

- Lack of histo-pathological correlation
- Buried columnar glands
- Risk of sub-squamous cancer
- Persistent genetic abnormalities (PDT)

BÀRRX RFA and CSA Cryotherapy

Role of Endoscopic Mucosal Resection (EMR)
- Accurate T staging (i.e. SM invasion)
- Aids histo-pathological evaluation
  - differentiation
  - lympho-vascular invasion

Trimodal Imaging assisted EMR

Histopathology evaluation
- Specialist GI pathologist
- Consensus diagnosis (at least 2 pathologists)
- Vienna classification to grade dysplasia (e.g. LGD)
- Degree of differentiation (e.g. well differentiated)
- Lympho-vascular invasion
- Immuno-histochemistry (e.g. P53 staining)
- SM invasion

EMR is the final step in diagnostic work-up and the first step in endo-therapy

Iterative Endoscopic Therapy for Barrett’s Early Cancer and HGD: Long-term Results in 379 patients.
- Complete remission achieved in 96%
- Recurrence / metachronous lesions 21%
- 5 year survival rate 84%
- Overall complications 15%
Lesions suitable for curative EMR in Barrett’s:

- HGD and intramucosal carcinoma
- Less than 3 cm in size
- Moderate or good tumour differentiation
- No lymphatic or vascular invasion


How to prevent metachronous lesions?

Circumferential EMR with cap or MBL

- Feasible and safe in ‘expert hands’
- Complete eradication of Barrett’s and neoplasia possible
- Technically difficult in long segments > 3cm


High stricture rate ~70%

Multi-modal therapy!
Radiofrequency energy ablation

RFA sham controlled study

- 127 patients with dysplastic Barrett’s (HGD 63, LGD 64)
- Only 11 patients had prior EMR for visible mucosal abnormality
- 2:1 randomisation (RFA vs sham)
- Randomisation stratified to dysplasia grade & Barrett’s length
- Primary outcomes at 12 months eradication of dysplasia and intestinal metaplasia
- Complete ablation 90.5% (81% HGD) Vs 22.7%,
- IM ablation 77.4% Vs 2.3%
- Ablation group fewer progression to cancer 1.2% Vs 9.3%
- AE: Chest pain common, 6% oesophageal stricture, 1% UGI bleed
- Drop out 7.9% (10 patients, 6 RFA, 4 sham)


EMR with RFA: multi-centre European trial

- 24 patients
- Eradication of neoplasia 100%
- Eradication of Barrett’s 96%
- No significant complications


55 yr old male with chronic heartburns and partial response to PPI undergoes endoscopy

EMR

EUS

EUS LN FNA

EMR with RFA: multi-centre European trial

EMR
**HGD with intra-mucosal Ca.**
Moderately differentiated
No lympho-vascular invasion

**HALO 360**

**HALO 90**

**Ideal endoscopic therapy**

- Accurate staging (EUS/EMR)
- Effective removal of metaplastic & dysplastic cells
- Replacement with normal squamous epithelium
- Safety for patients, nursing & medical staff
- Ease of learning and performing the technique
- Equipment inexpensive to purchase & operate
- Robust long-term follow-up
Summary

- Endoscopic therapy is now the preferred option for dysplastic Barrett’s.
- Endoscopic work-up is crucial for accurate staging and select appropriate patients.
- High resolution endoscopy should be the minimum standard, newer enhanced imaging techniques are complimentary.
- EMR is the final step in diagnostic work-up and first step in endoscopic therapy.
- RFA is emerging as an ideal ablation technique complimenting EMR for complete Barrett’s eradication.