



## Long term clinical outcomes in neoplastic Barrett's Oesophagus: A historical cohort study of early cases treated endoscopically at a tertiary referral centre

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### Background and Aims

Barrett's oesophagus (BO) is a premalignant, metaplastic change which may progress to oesophageal adenocarcinoma (OAC). Established endoscopic therapies (ETs) used to treat early neoplasia in BO include endoscopic mucosal resection (EMR) and radiofrequency ablation (RFA). The objective of this study was to determine the time and number of procedures to reach complete remission of dysplasia (CRD) and intestinal metaplasia (CRIM) in patients treated with ET for dysplastic BO or early OAC. Recurrence rates of metaplasia and dysplasia as well as adverse events related to endoscopic treatment were evaluated.

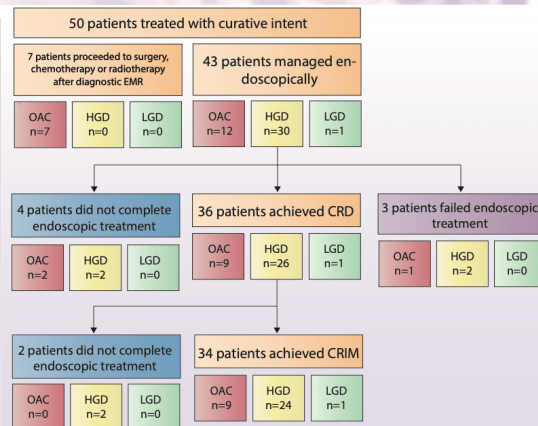
### Methods

We conducted a retrospective medical chart review of the first 50 patients identified from a departmental database of all BO patients treated for neoplasia at a single tertiary hospital between 2007 and 2020. Endoscopic, clinical, and histologic data were collected. Patients were followed up from index endoscopy to last procedure or death. This descriptive study summarises long-term clinical outcomes related to endoscopic treatment of dysplastic BO and early OAC. CRD and CRIM were defined as two consecutive endoscopies without dysplasia or metaplasia on histology. Baseline and outcome data were summarised using descriptive statistics, all of which was non-parametric and represented as median and interquartile range (IQR). Outcomes for those with OAC and high-grade dysplasia (HGD) at baseline were compared using Wilcoxon rank-sum tests, and Kaplan-Meier curves were created for time to CRD and CRIM.

### Results

	Treatment cohort n = 50
Age in years at diagnosis, median (IQR)	68 (61-73)
Male, n (%)	43 (86)
BMI, median (IQR)	29.4 (25.7-33.2)
<b>Tobacco use at index endoscopy, n (%)</b>	
Current	8 (16)
Ex-smoker	23 (46)
Never smoker	19 (38)
Family Hx OAC, n (%)	2 (4)
BO length of maximal extent in cm, median (IQR)	4 (2-9)
History of CVD, n (%)	14 (28)
PPI use at index endoscopy, n (%)	44 (88)
Aspirin use at index endoscopy, n (%)	16 (32)
Charlson Comorbidity Index, median (IQR)	3 (2-4)

Table 1: Baseline patient characteristics.



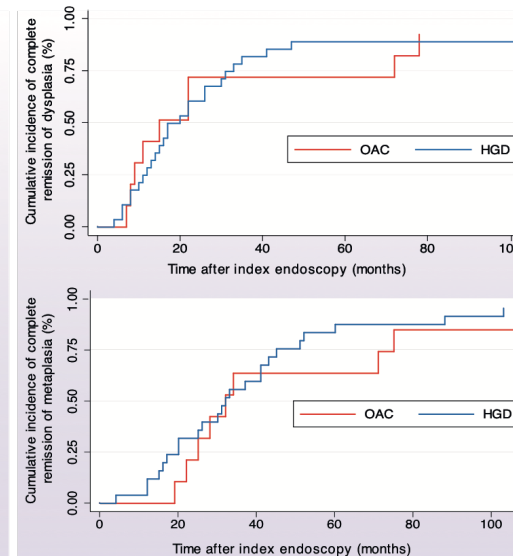
**Figure 1: Patient selection and results.** Fifty patients received primary ET with curative intent. Seven patients were referred on for radiotherapy, chemotherapy or surgery after a single diagnostic EMR. Forty-three patients were treated endoscopically, of which four patients (9%) did not complete treatment due to death from another cause or a clinical decision to cease active treatment in view of age or comorbidities. Of the 39 patients who continued endoscopic treatment, 36 attained CRD and 34 attained CRIM.

#### Patient demographics:

- Fifty patients received primary ET with curative intent.
- Initial treatment session for all patients was performed between December 2007 and June 2015.
- Median baseline BO length was 4 cm (IQR, 2-9) and highest degree of neoplasia was OAC in 19 patients (38%), HGD in 30 (60%) and LGD in one (2%).

#### Time to CRD and CRIM:

- Seven patients were referred on for radiotherapy, chemotherapy or surgery after a single diagnostic EMR due to adverse prognostic features on histology, while the remaining 43 patients were selected to continue endoscopic therapy.
- CRD was attained in 36 patients, representing 92% as per-protocol analysis and 84% by intention-to-treat analysis. CRD was reached within a median of 17 months (IQR, 10.5-30.5) and two procedures (IQR, 1.5-3.5; EMR 1 [0-2], RFA 1 [0-2]).
- CRIM was attained in 34 patients, representing 92% by per-protocol analysis and 79% by intention-to-treat analysis. CRIM was reached within a median of 32 months (IQR, 20-45) and three procedures (IQR, 2-5; EMR 1 [0-3], RFA 1 [0-2]).



**Figure 2: Kaplan-Meier curves of cumulative CRD and CRIM incidence.** Cumulative incidence of patients reaching CRD (upper panel) and CRIM (lower panel) over time since index endoscopy where dysplasia first diagnosed.

#### Recurrence, complications and mortality:

- Dysplasia recurred in six patients (17%) within a median of 10.5 months (IQR, 6-28), while metaplasia recurred in 12 (35%) within a median of 12.5 months (IQR, 8.5-35.5). OAC did not recur.
- Across a median follow-up of 99.5 months (IQR, 68-119), complications occurred in 19 patients (44%), all of which were managed endoscopically or conservatively.
- Stricture development was the most common complication and occurred in 16 patients (37%) and required a median number of 2.5 dilatations (IQR, 2-7.5). In addition, complications necessitating admission included three post-procedural bleeds, a contained perforation and an episode of pain.
- There were ten deaths (23%) among patients undergoing long-term ET, none of which were related to OAC.
- There was no statistically significant difference in outcomes or complications between patients with OAC or HGD at baseline.

	All patients n=43	LGD n=1	HGD n=30	OAC n=12
<b>Reached CRD, n</b>	36	1	26	9
% by protocol analysis	92	100	93	90
% by intention to treat analysis	84	100	87	75
<b>Time to reach CRD in months, median (IQR)</b>	17 (10.5-30.5)	39	17 (11-30)	15 (9-22)
<b>Number of procedures to reach CRD, median (IQR)</b>				
Total	2 (1.5-3.5)	2	2 (2-3)	3 (2-5)
EMR	1 (0-2)	2	0.5 (0-2)	3 (1-3)
RFA	1 (0-2)	0	1 (0-2)	0 (0-1)
APC	0 (0-0)	0	0 (0-0)	0 (0-0)
<b>Recurrence of dysplasia, n (%)</b>	6 (17)	0 (0)	6 (23)	0 (0)
<b>Reached CRD</b>				
Months between CRD and recurrence, median (IQR)	10.5 (6-28)	-	10.5 (6-28)	-
<b>Reached CRIM, n</b>	34	1	24	9
% by protocol analysis	92	100	92	90
% by intention to treat analysis	79	100	80	75
<b>Time to reach CRIM in months, median (IQR)</b>	32 (20-45)	44	31.5 (18.5-44)	32 (25-71)
<b>Number of procedures to reach CRIM, median (IQR)</b>				
Total	3 (2-5)	2	2.5 (2-4)	5 (3-5)
EMR	1 (0-3)	2	1 (0-2.5)	3 (1-4)
RFA	1 (0-2)	0	1.5 (0-2.5)	1 (1-1)
APC	0 (0-0)	0	0 (0-0)	0 (0-0)
<b>Recurrence of metaplasia, n (%)</b>	12 (35)	1 (100)	8 (33)	3 (33)
<b>Reached CRIM</b>				
Months between CRIM and recurrence, median (IQR)	12.5 (8.5-35.5)	51	9 (7-15.5)	32 (22-65.5)
<b>Follow up months, median (IQR)</b>	99.5 (68-119)	139	98 (63-110)	102.5 (71.5-128)
<b>Complications, n (%)</b>				
Total	19 (44)	1 (100)	12 (40)	6 (50)
Stricture development	16 (37)	1 (100)	11 (37)	4 (33)
Pain	1 (2)	0 (0)	1 (3)	0 (0)
Bleed	3 (7)	0 (0)	1 (3)	2 (17)
Perforation	1 (2)	0 (0)	1 (3)	0 (0)
<b>Number of dilatations required for patients with stricture, n (IQR)</b>	2.5 (2-7.5)	2	2 (1-7)	6.5 (2.5-12)

**Table 2: Outcomes and complications according to degree of dysplasia at baseline.** When comparing patients who had HGD or OAC at baseline, there was no statistically significant difference in outcomes or complications of ET.

### Conclusions

Our study reports on the long-term outcomes of patients with endoscopically treated neoplastic BO, with a median follow-up of over eight years. We demonstrate that even in this very early group, ET for neoplastic BO was effective, with a high proportion of patients reaching CRD and CRIM. There were no cases of OAC recurrence after CRD, and none of the patients who were selected to continue with ET after an initial diagnostic EMR died from OAC. There was no difference in outcomes between patients with OAC or HGD at baseline, suggesting that patients with early OAC are being appropriately selected for and can be safely managed with ET. The safety profile was favourable, with the main adverse event being stricture development.