Appendix 5

Summary of relevant evidence from the Cochrane Review on Barrett's Oesophagus (Rees 2010)

Objectives of the review: To summarise, quantify and compare the efficacy of treatments to induce reversal of Barrett's oesophagus or dysplasia or to halt the progression to cancer. Three main groups of therapeutic interventions were considered (only RCT evidence was considered):

1. Pharmacological treatments: H2-receptor antagonists, proton pump inhibitors, prokinetics and antacids, as well as chemopreventive agents such as NSAIDs, aspirin and COX-2 inhibitors.

2. Anti-reflux procedures. The surgical treatments have been compared with each other or with pharmacological treatment if these data are available.

3. Endoscopic ablative methods: thermal (argon plasma coagulation, multipolar electrocautery, laser therapy, cryotherapy and radiofrequency ablation), chemical (photodynamic therapy) and mechanical methods (endoscopic mucosal resection and ultrasonic surgical aspiration).

So only the objective 3 is relevant to the scope of this guideline and the included studies for this section were:

Study ID	Included/ excluded and reason for exclusion
Ackroyd 2000	Only included LGD population
Bright 2007	Only included non-dysplastic BO
Dulai 2005	Excluded HGD or CA population
Hage 2004	Only included non-dysplastic BO (32) and LGD (8)
Luman 1996	Only included non-dysplastic BO
Mackenzie 2008	Valid population but available only in abstract form and therefore not included in our review. The study compares 5-ALA versus porfimer sodium; summary available*
Overholt 2005-2007	*Included*
Peters 1999	Excluded HGD or CA population

Ragunath 2005	Excluded by GDG, for further information please refer to section 2.4.1
Shaheen 2008	*Included*
Sharma 2006	Excluded HGD or CA population

*****Mackenzie 2008

Mackenzie 2008 randomised 32 patients, stratified per length of segment, to 5-ALA (n = 16) or porfimer sodium (n = 16).The authors stated that they used the standard protocol (no more details available) and 60 mg/kg 5-ALA, activated by 1178 J/cm of red laser light. Patients were then followed up with quadrantic biopsies every 2 cm at six weeks, four months and one year post-therapy.

1) **Outcome: Eradication of HGD**: 5-ALA 14/14 vs. Photofrin 9/14: OR= 16.79 [0.83, 340.08] **NS**

2) **Outcome: Stricture:** 5-ALA 1/16 vs. Photofrin 6/16: OR= 0.12 [0.01, 1.09] **NS**

Evidence tables of included studies

Table 1 Evidence Table for included endotherapy studies

Study ID	Aim	Study design	Follow- up	Population	Intervention	Comparison	Outcome(s)	Comments
Das, 2008	To study the cancer-free survival in patients with early oesophageal cancer managed with either endoscopic therapy or surgical resection	Retrospective cohort study	mean 23.9 months for endotherapy group and mean 25.3 months for surgery group	621: Early oesophageal adenocarcinoma (stage T1 and T0); endoscopic procedures (n=99) vs surgery (n=643)	Endoscopic therapies: ER alone 65 (65.7%) ER+PDT 10 (10.1%) ER+thermal ablation (Laser+APC) 4 (4.0%) PDT alone 11 (11.1%) Thermal ablation alone 5 (5.1%) Ablative therapy (not otherwise specified) 4 (4.0)	surgery	**Efficacy:** Survival: In the Cox proportional hazards model, the relative hazard for oesophageal cancer-specific mortality in endotherapy group was not different from that of surgery group (relative hazard [RH] 0.89, 95% confidence interval [CI] 0.51–1.56, P = 0.68). The significant predictors of survival were age at diagnosis (RH 1.06, 95% CI 1.03–1.08, P < 0.001) and absence of exposure to radiation therapy (RH 0.32, 95% CI 0.21–0.48, P < 0.001) The median cancer-free survival (calculated by Kaplan-Meier estimate) in the endotherapy group was not significantly different from that in the surgically treated group (56 and 59 months, respectively, P=0.41)	A retrospective analysis of cases identified from a national registry. Participant characteristics were studied between the two groups with the surgical group being significantly younger, with stage 1 disease and with sub mucosal invasion. Kaplan Meier estimates were done for median cancer-free months of 56 (50-61) for endotherapy arm and 59 (57-67) for

Study ID	Aim	Study design	Follow- up	Population	Intervention	Comparison	Outcome(s)	Comments
								surgery arm.

Study ID	Aim	Study design	Follow- up	Population	Intervention	Comparison	Outcome(s)	Comments
Greenstein 2008	To assess the relationship between local endoscopic therapy and survival for early oesophageal cancer	cohort study	Median 17 mths (range 1 - 69)	T0-T1 oesophageal cancers; Adenocarcinomas =100: Local procedures (n=47) vs no therapy (n=119)	Local procedures versus no therapy Excisional biopsy 19 (40%) Photodynamic 11 (23%) Local destruction (NOS) 6 (13%) Laser therapy 5 (11%) Polypectomy 3 (7%) Electrocautery 1 (2%) Cryoablation 1 (2)	no therapy	**Efficacy:** Survival (4 yr disease-specific) rate **-** 84% (95% CI 71 to 96%) local therapy; 64% (95% CI 54 to 74%) no therapy; p<0.01 (difference remained after baseline adjustment, p=0.04) Non-oesophageal cancer survival rates similar (p=0.22), suggesting no differences in burden of disease Multivariate analysis showed HR 0.39 (95% CI 0.16 to 0.96, p=0.04) with local therapy c.f. no therapy ; 1.42 (95% CI 0.66 to 3.08, p-0.37) female c.f. male ; 0.59 (95% CI 0.20 to 1.71) aged 60-70 or 1.70 aged over 70 (95% CI 0.68 to 4.23, p=0.25) c.f. aged under 60; 0.45 married (95% CI 0.22 to 0.92, p=0.03) c.f. not married; 1.14 (95% CI 0.37 to 3.55, p=0.82) or 2.22 hispanic (95% CI 0.80 to 6.19, p=0.13) or 0.24 (0.03 to 2.09, p=0.20) c.f. white; 1.12 SCC (95% CI 0.46 to 2.73, p=0.80) or 0.60 other cell type (95% CI 0.19 to 1.84, p=0.37) c.f. AC; 1.92 T0 (95% CI 0.96 to 3.84) c.f. T1; 1.49 middle (95% CI 0.65 to 3.44, p=0.35) or 2.76 upper (95% CI 0.73 to 10.45, p=0.14) or 1.36 not reported (95% 0.48 to 3.83, p=0.57) c.f. lower oesophagus.	A retrospective analysis of cases identified from a national registry of incident cancers. Excluded those who underwent resection or radiation therapy. Authors reported limitations were the lack of clinical information (co morbidities, diagnostic assessment, lesion details etc) and the inability to be confident that patients who received chemotherapy were excluded. Authors reported strengths included the large sample size and the generalisability. Also the database is quality assured.

Study ID	Aim	Study design	Follow- up	Population	Intervention	Comparison	Outcome(s)	Comments
Manner, 2006	To study safety and efficacy of APC therapy after previous endotherapy for Barrett's oesophagus and early cancer	case series	Not stated	215: analysis on 190 and BO 111 (BO early cancer)	APC: hp-APC using VIO 300 D Pulsed at 16/s but previously had ER or ER+PDT	None	**Efficacy:** 41/111 had prior ER to remove BO early cancer. To achieve complete ablation 1.1±0.4 (1-2) treatments were needed using mean wattage 59±3.3 (50-60). In 70/111 had prior ER / PDT and achieved complete ablation 1.3±0.4 (1-3) treatments were needed using mean wattage 73±4.4 (50-60). Overall 1.2 (1-3) treatment at 68 (50-80) W. **Adverse effects (AES):** of 41 patients: Minor complications 8/41 (4 chest pain; 4 fever) and major 1/41(stenosis). Of 70 patients: Minor complications 5/70 (3 chest pain; 2 fever) and no major AES	Single centre study, mainly looking at safety/ adverse events.
Manner, 2007	To study the safety and efficacy of APC therapy after previous endotherapy for Barrett's oesophagus and early cancer	case series	Not stated	216: 131 BO and early cancer); 1 high grade intraepithelia neoplasia + 22 cases of early BO cancer.	APC: hp-APC using VIO 300 D Pulsed at 16/s with changing power setting from 30-80 W but previously had ER or ER+PDT		**Efficacy:** Of 131 patients, 104 had no intraepithelial neoplasia. Mean wattage 52±5.3 (30-60). 27 cases had low grade intraepithelial neoplasia (5) or early BO cancer (22). Mean treatment wattage used was 61.9±11.1 (50-80) W. Overall 1.1 (1-5) treatments at 54 (30-80) W. **Adverse effects:** For all BO: Minor (pain, dysphagia, cough after APC, cardiac arrhythmia, gas accumulation in GI wall, neuromuscular irritation)=14/131 and Major: Stenosis =1/131 For early cancer BO: neuromuscular irritation 1/22; complications by W seen at 30W=0/2; 50 W=7minor+1major (8)/87; 60W=4minor/31; 70W 3minor/7; 80W=0/4	Single centre study, mainly looking at safety/ adverse events.

Study ID	Aim	Study design	Follow- up	Population	Intervention	Comparison	Outcome(s)	Comments
May 2002a and 2002b	To study the safety and efficacy of endotherapy for high grade Barrett's or and early oesophageal cancer	prospective case series	34 ±10 months (range 24-60 months)	115: HG neoplasia and 96 early adenocarcinoma: ER n= 70 PDT n=32 ER+PDT = 10; primary treatment with APC =3	APC (only initial phase for small lesions); ER (when possible to localise early CA or HG); PDT using 5-ALA for HG (n=26) and CA of 2mm or mTHPC (meta-tetra-hydroxyphenyl-chlorine) >2mm CA (n=4); with both (n=2)	none	**Efficacy:** 4 had surgery and 1 died before completion of treatment (myocardial infarction) so 108 per protocol/ 110 IIT. CLR (complete local remission) =108/115 or 108/110 [ER=65/66; PDT=32/32; ER+PDT=8/9; APC=3/3); LET (failure of local endoscopic therapy) =2; ER=1/66; ER+PDT=1/10); Survival rates (life tables): 1yr 98%; 2yr 95%; 3 yr 88%. **Adverse effects:** Death: occurred in 13/110; 6 From cardiovascular; 5 due to second neoplasia; 1 liver cirrhosis; 1 Barrett's adenocarcinoma; no severe complications- Minor complications:11/115; (7/70; PDT: 1/32; ER+PDT=3/10; 3/3): included stenosis (3), bleeding (5), odynophagia (1) and photosensitive reaction-sunburn (2).	Long term study, showing survival analysis but using life-tables and limited use of IIT principle. Compares ER/ PDT/APC.

Study ID	Aim	Study design	Follow- up	Population	Intervention	Comparison	Outcome(s)	Comments
Pech 2008	Short term and long term study using endotherapy for high grade intraepithelial neoplasia and mucosal adenocarcinoma	case series	Median 63 mths (inter-quartile range 49.5 to 80.0)	486 with suspected IEN or early AC: 349 with HGIN (61) and mucosal BC (288)	Nd: YAG laser was done in patients with >stage 1 tumours but in whom chemotherapy or surgery was not possible. ER "suck and cut" with ligating device or cap; n=279, 734 resections; piecemeal in 100/279 (35.8%) due to neoplastic lesions diameter < 2cm; PDT; n=55, wide areas of superficial neoplasia or when proven neoplasia could not be detected (n=10) ER+PDT; n=13, PDT to ablate remaining areas APC; n=2, very small areas of neoplasia	None	**Efficacy: Complete local remission -** 337/349 (96.6%) median of 4.2 (S.D. 5.6) months; 184 during initial endoscopies and 95 in repeat endoscopies. Mean ER per patient 2.1. Long term complete response 330/349 (94.5%) Failure of treatment - 13 (3.7%) underwent surgery **Progression to advanced disease -** metachronous lesions detected in 74 patients at a median of 15 months. 63/74 achieved complete remission after repeat treatment; 3 referred for surgery; 2 received ongoing therapy; 2 died. **Recurrence free rate -** 77% at 5 years. No sig difference between different tumour stages. Recurrence associated with long-segment Barrett's oesophagus RR 1.9 (95% CI 1.06 to 3.3) p=0.03; time until CLR achieved >10 months RR 0.3 (95% CI 0.12 to 0.75) p=0.009; piecemeal resection RR 2.44 (95% CI 1.13 to 4.89) p=0.02; multifocal neoplasia RR 2.1 (95% CI 1.16 to 3.99) p=0.01 ; no ablative therapy of Barrett's oesophagus after CLR RR 2.5 (95% CI 1.52 to 3.85) p=0.0003. No sig association for tumour stage, macroscopic type, lesion size ≤2 or > 2cm, or treatment modality. **Survival rates** - overall 5 year survival rate 84%. No sig difference between different tumour stages. **Complete local remission (mucosal cancer with ER alone)** - 225/231 (97.4%) at median 3 months. 221/231 (95.7%) long term. **Progression (mucosal cancer with ER alone)** - metachronous lesions detected in 49 patients (21.2%) **Survival rates (mucosal cancer with ER alone)** - 201/231 (87%) survival at 61 months median follow-up. 30 (13%) died of other causes	Large, well documented, prospective case series. Single site. No control. Complete local remission (CLR) defined as R0 resection plus 1 normal endoscopic exam; or R1/X 2 consecutive endoscopic exams - if failed then underwent oesophagectomy. Data on treatment of non-neoplastic BO remaining not reported as not relevant for this scope.

Study ID	Aim	Study design	Follow- up	Population	Intervention	Comparison	Outcome(s)	Comments
Peters 2005a; 2005b	To evaluate the efficacy of photodynamic therapy (PDT) in the treatment of residual high-grade dysplasia or early cancer (HGD/EC) in Barrett's oesophagus (BO) after endoscopic resection.	case series	Median follow-up of 30 months (22-31 months) .	34 for ER, Three of these patients were then treated with APC and 20 patients treated with PDT. Group A consisted of 11 patients with proven residual HGD/EC in BO after ER. Group B was nine patients with possible residual HGD/EC in BO after ER.	Ablation with PDT using 5-aminolevulinic photosensitization plus APC following ER	None	**Efficacy:** After PDT, complete local remission was achieved in 15 (75%) patients. Group B patients (100%) reached complete local remission compared with 6 out of 11 (55%) of group A patients (p = 0.03; Fisher exact test). Of the five patients with persisting HGD/EC after PDT, two were referred for surgery, endoscopic resection plus APC (n = 1), endoscopic resection plus PDT (n = 1), and PDT plus APC (n = 1). The three reached complete local remission. Overall, endoscopic treatment resulted in complete local remission in 18/20 patients (90%). At 3 months after PDT, patients had residual Barrett's mucosa at endoscopy; median regression percentage was 50% (25 - 70%) in group A and 55% (30 -75%) in group B. **Adverse effects:** Complications observed in 4 patients. Haematemesis in one patient, one week after PDT. Two patients had a 5-ALA-induced hypotensive episode after the procedure and one patient suffered an episode of atrial fibrillation 6 hours after PDT.	No death during follow-up. Most patients undergoing 5-ALA-PDT have residual Barrett's mucosa after PDT and 5-ALA-PDT does not seem to prevent recurrences during follow-up. Population not clearly defined. .

Study ID	Aim	Study design	Follow- up	Population	Intervention	Comparison	Outcome(s)	Comments
Prasad, 2009	To compare long-term outcomes of patients with mucosal oesophageal adenocarcinoma treated endoscopically and surgically.	cohort study	mean follow-up 64 months (standard error of the mean, 4.8 months) in the surgical group and 43 months (standard error of the mean, 2.8 months) in the endotherapy group	178: 132 patients in the endoscopic therapy group (ENDO group) and 46 patients in the oesophagectomy group (SURG group) for mucosal oesophageal adenocarcinoma between 1998 and 2007 at the Mayo Clinic (Rochester, MN) were included. Endotherapy: ER alone 75 (57%) ER+PDT 57	Endoscopic therapies: ER alone and ER+PDT	surgery	ENDO group: Remission was achieved successfully in 124 patients (94%) using ER and/or PDT. There was no statistically significant difference in the rate of achieving remission between the ER group and the ER+PDT groups. Eight patients elected to undergo oesophagectomy before remission could be achieved. The cumulative mortality was 17% (23 of 132) in the ENDO group and 20% (9 of 46) in the SURG group (P=0.75). Overall survival at 5 years was 83% in the ENDO group and 95% in the SURG group. The incidence rate ratio for overall mortality was 1.32 (ENDO group vs SURG group). Cancer-free survival was 80% at 5 years in the ENDO group and 97% in the SURG group. Using Coxproportional hazards modelling, overall survival was comparable between the 2 groups after adjusting for age, sex, length of BE segment, Charlson co morbidity score, and the propensity score, whereas cancer-free survival was superior in the SURG group (overall survival HR=1.54 (95%CI 0.64–3.75) p=0.33; cancer-free survival HR=2.64 (95%CI 1.70–4.08) p<0..001). ENDO group: Overall complication rate of 13% (18 of 132); eight patients developed strictures (all of whom had received PDT). All were treated successfully using endoscopic dilation with a median of 2 dilations needed to treat strictures. Five patients developed clinically significant bleeding needing hospitalisation. 5 patients developed mild photosensitivity. SURG group: Four had evidence of metastatic lymphadenopathy (8.6%) and	Good comparative study, with survival analysis and adjusting done for baseline characteristics.

Study ID	Aim	Study design	Follow- up	Population	Intervention	Comparison	Outcome(s)	Comments
Schembre 2008	To compare endoscopic therapy to oesophagectomy	cohort study	ET: median 20 months (range 6 to 84) Surgery : median 48 months (range 6 to 88)	117 with BO with HGD or IMC. 62 had endotherapy (ET) (48 HGD; 13 IMC) - 2 APC - 18 ER - 2- PDT - 22 ER and PDT - all had some APC during follow-up + 32 had surgery (15 HGD; 17 IMC) - 4 transhiatal; 10 Ivor-Lewis - 18 left thoracoabdominal	ET PDT, ER, APC or any combination PDT with porfimer sodium for primary treatment of HGD/IMC 1998-2000 ER for focal disease with PST for residual BO 2000-3 ER for large area BO <5cm with PDT for BO>5cm 2003 onwards APC for small area or residual disease Surgery - single surgeon, with pre-op and cardiac testing. Resection individualised according to patient physiology and characteristics.	surgery	**Efficacy:** Complete remission (no BO) - 35/62 (56%) (reported as residual BO so calculated back) ET; 31/32 (97%) surgery; p<0.001 Partial remission (no dysplasia) - 54/62 (87%) (reported as persistent dysplasia so calculated back; undergoing further therapy) ET; 31/32 (97%) surgery; p=0.12 Progression to cancer - 4/62 (6%) ET (2 IMC 2 invasive); 0/32 (0%) surgery; p=0.14 Overall survival rate (4 year adjusted) - 89% ET; 93% surgery; p=0.49 Procedure related mortality - 1/62 (2%) ET; 0/32 (0%) surgery; p=0.47 **Adverse effects:** Major complications - 5/62 (8%) ET (death 1; bleeding 2; prolonged hospitalisation 3); 4/32 (13%) surgery (anastomatic leak 1; chyle leak 2; DVT 1); p=0.50 Minor complications - 20/62(32%) ET (stricture 13; photosensitivity 4; pneumonia 2); 26/32 (66%) surgery (pneumonia 2; atrial fibrillation 6; wound infection 3; stricture 15; pneumothorax 1); p<0.001	Two institutional review board approved prospective databases - analysed retrospectively.

Table 2 Evidence Table for included ER alone studies

Study ID	Aim	Study design	Follow- up	Population	Intervention	Comparison	Outcome	Comments
Conio 2005	To evaluate ER, specifically in terms of complications and recurrence rate	Case series	34.9 months	Histologically confirmed HGD or IMC in BO. N=39 total 35 with HGD 4 with IMC	ER	None	Mis-staging of 10/39; **Adverse effects:** Bleeding: 4/39 patients; 1/39 stenosis	Standard case series
Ell, 2000; 2007	To determine the long term effects of ER with curative intent	Prospective case series	In 2000: mean 10±8 months (2-25 months); 2007: mean 36.7 months ±15.45; median 33 months (2-83 months)	In 2000: 64High grade dysplasia (n=29) and early carcinoma (n=35); In 2007: low-risk oesophageal cancer (n=100): consecutive 100 patients	ER "suck and cut" technique with using a ligation device or with a cap system.	None	**Efficacy:** Complete local remission - 99/100 (99%); achieved after 1 resection in 70 patients, after 2 in 20, 3 in 6, 4 in 1, and after 5 in 3. Mean ER per patient 1.47. Progression to disease - metachronous lesions detected in 11 patients (11%); local recurrence n=6, different location in Barrett's segment n=5. All successfully treated with ER to CLR. Survival rates - estimated probability 99% at 1 year, 99% at 2, 98% at four, and 98% at five years. **Adverse effects:** No major complication was observed. Acute: no severe complications (perforation, bleeding with Hb>2g/dL or required transfusion) or	Large, well documented, prospective case series. Single site. Complete local remission (CLR) defined as R0 resection plus 1 normal endoscopic exam; or R1/X 2 consecutive endoscopic exams - if failed then underwent oesophagectomy. Treatment also failed if CLR not achieved after 5 consecutive ERs.

Study ID	Aim	Study design	Follow- up	Population	Intervention	Comparison	Outcome	Comments
							death; minor complications (haemorrhage post ER n=11) treated with diluted epinephrine Long-term: no strictures observed.	
Giovanni 2004	To evaluate the efficacy of circumferential ER	Prospective case series	18 months (6-34 months)	BO with preprocedure biopsy diagnosis of HGD or intraepithelial carcinoma. n=21 total 12 with HGD 9 with mucosal cancer	ER	None	**Efficacy:** 18/21 successfully ablation; 2 patients had local recurrence but treated successfully again with ER (at 8 months and 13 months); **Adverse effects:** 4 bleeding	1-3 ER sessions
Inoue 1991	To describe clinical applications of new technique	Case series	15 months	Early stage oesophageal cancer. n=4 total 1 with adenocarcinoma	ER - transparent tube	None	No recurrences, no complications	Study focusing on technique and not outcomes

Study ID	Aim	Study design	Follow- up	Population	Intervention	Comparison	Outcome	Comments
Inoue 1998	To evaluate the efficacy of ER	Retrospective case series	Max 9 years	142; 72% (102) with indications for ER (mucosal cancer); remainder poor risk of surgery or refused	ER-cap	None	**Efficacy:** no local or distant metastasis at follow-up Survival rates - 95% at five years; others died from MI, liver cirrhosis, apoplexy; **Adverse effects**: Acute: 1 perforation (treated and healthy 7 years later); 1 stenosis (not resolvable by dilation, treated with surgery)	Large case series, but very limited information on study methods. More information on ER. Not clear if the patient population is directly relevant.
Larghi 2007	To report long-term results of complete eradication of BO	Prospective case series	28 months (15-51 months)	26 with analysis for 24. BO with diagnosed HGD or IMC Excluded if disease was not confined to the mucosa (T1m) or had evidence of suspicious lymph nodes	ER	None	**Efficacy:** Median of 3 sessions (1-8) to remove 44 lesions. 21/24 had successful ablation; **Adverse effects** 3/24 stricture requiring 1 dilation; 2/24 bleeding	Standard case series

Study ID	Aim	Study design	Follow- up	Population	Intervention	Comparison	Outcome	Comments
Lopes 2007	To evaluate the efficacy of circumferential ER	Retrospective case series	31.6 months	N=41 total BO with HGD or early CA	ER - circumferential	None	**Efficacy:** 31/41 successful eradication of BO; **Adverse effects** Bleeding 8/41; 2/41 perforations; 1/41 stricture; BO recurred in 10 and CA in 5	Standard case series
Nijhawan 2000	To study diagnosis and treatment using ER	Retrospective case series	14.6 months (4-42 months; median 10)	N=25 total 13 (52%) with superficial AC 4 (16%) with HGD 8 (40%) with other low-risk lesions. Barrett's oesophagus with focal lesions ER only considered for uT0-uT1, confined to the mucosal layer, without evidence of lymph node metastases	ER if failed then PDT or surgery	None	**Efficacy:** 11/25 ER was curative; **Adverse effects** no complications but bleeding was not recorded	Study focusing on diagnostic efficiency of ER rather than curative

Study ID	Aim	Study design	Follow- up	Population	Intervention	Comparison	Outcome	Comments
Peters 2007	To prospectively evaluate the feasibility of multiband mucosectomy (MBM) for widespread ER in patients with a Barrett's oesophagus with early neoplasia and compare results retrospectively with prospectively registered endoscopic cap resection procedures	Prospective, comparing techniques of ER	Immediate, only procedure complications	N=93 total 40 with MBM 53 with cap ER. Barrett's oesophagus with HGIN or early cancer	ER with MBM or cap	None	**Adverse effects** 1 perforation in cap group; bleeding in 6% MBM and 20% cap group	Technical procedure summary and no relevant clinical outcomes reported. Safety data available
Prasad 2007	To describe the feasibility and efficacy of ER in patients with hypertension and BO	Retrospective case series	1- 4 months	N=4 but 3HGD Barrett's oesophagus and 3 HGD and 1 LDG	ER, RFA or PDT on failure	None	**Efficacy:** successful ablation in 1 and failure in 2; 1 with non dysplastic BO	List of individual case reports

Study ID	Aim	Study design	Follow- up	Population	Intervention	Comparison	Outcome	Comments
Seewald 2003	To study the effectiveness and safety of circumferential ER by simple snare technique without cap	Prospective case series	9 months	N=12, Multifocal HGD and/or IMC in Barrett's oesophagus	ER - circumferential	None	**Efficacy**: 12/12 successful ablation in median 2.5 ER sessions; **Adverse effects** strictures 2/12; and 4/31 sessions had bleeding	Standard case series
Soehendra 1997	To study the endoscopic snare technique	Case series	median 7 months (3-22)	N=7. Early oesophageal cancer	ER - snare resection	None	**Efficacy:** Complete eradication of BO in 7/7 cases with 1 session; **Adverse effects**: 2 patients underwent surgery after unsuccessful treatment and 2 others died from cardiac disease	Standard case series
Soehendra 2006	To study the feasibility of modified MBL device in facilitating circumferential ER of Barrett's oesophagus that contains high-grade intraepithelial neoplasia (HGIN) and/or intramucosal cancer (IMC)	Case series	Immediate, only procedure complications	N=10 consecutive patients Barrett's oesophagus with HGIN and/or IMC	ER - MBL	None	**Adverse effects:** strictures in 7/10 and bleeding in 2/10	Does not look at ablation of BO and/ or progression to cancer but only adverse events

Study ID	Aim	Study design	Follow- up	Population	Intervention	Comparison	Outcome	Comments
Thomas 2009	To determine the efficacy (lateral and deep margin clearance) of trimodal imaging endoscopy-assisted ER in early Barrett's neoplasia in a tertiary referral setting	Prospective case series	median 8 months (IQR 6-12 months)	N=16 total 13 with HGD 3 with IMC Barrett's related HGD or IMC	ER	None	**Efficacy:** 12/16 had complete ablation of BO; **Adverse effects:** 3/16 had bleeding	Standard case series

Table 3 Evidence Table for included APC alone studies

Study ID	Aim	Study design	Follow- up	Population	Intervention	Comparison	Outcome(s)	Comments
Attwood 2003	To study the long-term outcome of patients who have undergone endoscopic Argon ablation for HGD in Barrett's	case series	up to 7 years, mean 37 months, (7-78 months)	N= 29; HGD in BO	Argon, using ERBE beamer 2, at 2L/min flow and 70 watts	None	**Efficacy:** Complete ablation of BO: 22/29 (75.86%); Progression to cancer: 4/29 (14%); Survival**:** over 82% at 5 years; No deaths from oesophageal cancer; (3 unrelated deaths); **Adverse effects:** Strictures: 0/29; perforations: 1/29	Does survival analysis using Kaplan-Meier curves and life table estimates of survival comparing with standard (general) UK population

Study ID	Aim	Study design	Follow- up	Population	Intervention	Comparison	Outcome(s)	Comments
May, 1999	Case reports of 3 patients treated with endoscopic Argon ablation for proven early adenocarcinoma of Barrett's	case series of 3 case reports	25 months, 23 months and 6 months followed by PDT	N=3; proven early adenocarcinoma of Barrett's	Argon, using ERBE beamer 2	None	**Case 1**: 2 sessions of APC gave complete ablation of BO and carcinoma; **Case 2:** 2 APC treatments gave complete ablation of BO and carcinoma; **Case 3:** recurrence seen after 6 months so given PDT with 5-ALA (treatment failure) CR-IM/BO 2/3 (75%)	Series of case reports rather than overall results
Laethem, 2001	To study the endoscopic therapy of HGD and superficial adenocarcinoma associated with Barrett's using APC	Prospective case series	median follow-up of 24 months (range 12-36 months)	Histologically proven HGD or in situ cancer. N=10: 7 HGD and 3 in situ cancer10	Argon, using ERBE beamer 2	None	**Efficacy:** Complete eradication of dysplasia/ cancer: 8/10 patients (80%) mean number of 3.3+/-1.5 APC sessions; Complete ablation of BO: 5/10 (50%); Mortality**:** 1/10 within 2 years	Standard case series

Table 4 Evidence Table for included Laser therapy alone studies

Study ID	Aim	Study design	Follow- up	Population	Intervention	Comparison	Outcome(s)	Comments
Gossner, 1999	To report first results of ablation of BO using laser therapy	case series	mean 15 months (up to 10.6, no minimum)	Histologically proved BO. Total of 10: LGD=4; HGD=4 and early cancer =2	KTP laser (KTP/YAG XP 800) system at 12-18 W, 300-1000 J	None	**Efficacy:** Complete eradication of BO: 10/10 with 8 using PPI and 2 laparoscopic fundoplication apart from laser. An average of 2.4 treatments was needed for ablation. Absence of dysplasia was maintained for 15 months of study. **Adverse effects:** Retrosternal burning pain = 3/10	Standard case series

Study ID	Aim	Study design	Follow- up	Population	Intervention	Comparison	Outcome(s)	Comments
Mathus-Vliegen, 1990	Treatment with Nd:YAG laser photocoagulation was analyzed in retrospect to identify factors relating to failures and complications of laser therapy	Retrospective case series	8 years	378 patients with 21 with of upper GI cancer. Patients with benign and malignant GI tumours	neodymium: YAG laser (power 100 watts, pulsed at 0.1-9.9 seconds)	None	**Adverse effects:** Bleeding: 3/21; Retrosternal burning pain: 7 occasions; no perforations or mediastinitis	Large retrospective case series, with very limited specifics for relevant population and may not be early adenocarcinoma
Weston, 2000	To study the efficacy and safety of neodymium:yttrium-aluminum garnet (Nd:YAG) contact laser ablation of Barrett's HGD and/or early adenocarcinoma	Case series	mean 12.8±6.5 months; 2 months-36 months	Total of 36: with 17 meeting inclusion criteria and analysis done in 14. Patients with Barrett's in whom HGD; HGD with IMC and/ or adenocarcinoma	neodymium:yttrium-aluminum garnet (Nd:YAG) contact laser	None	**Efficacy:** Complete eradication of HGD and CA: 14/14; Complete eradication of BO: 11/14 (78.6%); **Adverse effects:** Stricture: 2/14 and mild upper GI bleed: 1/14	Study follows 36 patients based on their staging and treatment options

Table 5 Evidence Table for included laser + MPEC studies

Study ID	Aim	Study design	Follow- up	Population	Intervention	Comparison	Outcome(s)	Comments
Sharma 1999	Long term follow-up	prospective case series	median 3.4 years (9-86 months)	N=6; Biopsy proven Barrett's with IMC	Laser (Nd:YAG laser) and MPEC	None	**Efficacy:** Overall ablation of Barrett's 2/6 with a mean of 2.8 laser sessions and 3.3 MPEC sessions	Long term follow up over 7 years
Sharma 2000	To evaluate the outcome of HGD in patients with Barrett's undergoing ablation with laser and MPEC	Prospective case series	median 12 months (4-27 months)	N=8; Barrett's with HGD	Laser (Nd:YAG laser) and MPEC	None	**Efficacy:** Overall ablation of Barrett's 3/8	Abstract only

Table 6 Evidence Table for included APC + MPEC studies

Study ID	Aim	Study design	Follow- up	Population	Intervention	Comparison	Outcome(s)	Comments
Sampliner 2006	To report cases of progression to cancer	Prospective case series	5, 14 and 24 months	N=3; HGD of BO	MPEC and Argon	None	**Efficacy:** All progressed to cancer	Individual case reports of special cases of progression to adenocarcinoma after ablation

Table 7 Evidence table for included RFA studies

Study ID	Aim	Study design	Follow- up	Population	Intervention	Comparison	Outcome(s)	Comments
Ganz, 2008	To study the efficacy of RFA in the treatment of high-grade dysplasia for Barrett's	Case Series	up to 3 years (median 12 months)	142, all HGD for Barrett's	RFA circumferential ablation - HALO^{360}	None	**Efficacy:** Efficacy data available for 92/ 142 patients, CR-D 80.4%; CR-IM 54.3%; CR-HGD 90.2% Subgroup analysis available: Prior ER (n=24) vs. no Prior ER (n=68): CR-D 81.3% vs. 80.3%; CR-IM 62.5% vs. 52.6%; CR-HGD 87.5% vs. 90.8% **Adverse effects:** No serious AES; safety data available for 142 patients; 1 stricture in asymptomatic patient that required no dilation; 2 patients under went oesophagectomy after 3 months	Large case series, patient registry from 16 institutions, with confirmed HGD BO, Sub group analysis with and without ER available, but majority (74%) with RFA alone

Study ID	Aim	Study design	Follow- up	Population	Intervention	Comparison	Outcome(s)	Comments
Shaheen, 2009	To study effectiveness of RFA in treatment for Barrett's oesophagus	RCT	12 months	127; but HGD (relevant population) =63: RFA (n=42) vs. Sham (n=21)	RFA versus; circumferential ablation - HALO^{360} (four applications per session).	Sham procedure	**Efficacy:** Complete eradication of Dysplasia - RFA 34/42 (81%) vs. 4/21(19%); RR=4.2 (1.7-10.4); NNT=1.6 Complete eradication of intestinal metaplasia - RFA 31/42 (74%) vs. 0/21 (0%); NNT=1.4 Progression of dysplasia/ disease to cancer - RFA 1/42 (2%) vs. 4/21 (18%); RR=0.1 (0.01-1.0); NNT=1.6 Biopsy free of intestinal metaplasia at 12months - 1442/1464 (98%) vs. 360/614 (59%); RR=1.7 (1.6-1.8) **Adverse effects:** results from 298 treatments in 84 patients; 3 serious AES in RFA vs. 0 in control; (1 upper gastrointestinal haemorrhage, 1 chest pain after 8 days and 1 chest discomfort and nausea immediately after procedure); 0-100 VAS score HGD - RFA (n=41) median 22 vs. 0 control (n=20)	Large 19 sites US RCT with 80% power to detect a 50% difference, stratified randomization by grade of dysplasia and length of Barrett's oesophagus, clear inclusion and exclusion criteria, appropriate blinding, appropriate primary and secondary outcomes, good explanation of techniques and patient follow up (CONSORT available). Acceptable follow up but longer would show long term effectiveness and adverse events, no sub group division for adverse events; authors state that statistical significance in rate of progression to cancer would be lost with only 1 more individual in the control group and therefore results should be considered with caution.

Table 8 Evidence table for included PDT alone studies

Study ID	Aim	Study design	Follow-up	Population	Intervention	Comparison	Outcome(s)	Comments
Ackroyd; 1999	To evaluate the efficacy of Aminolaevulinic Acid (5-ALA) induced Photodynamic therapy in the treatment of dysplatic BO and adenocarcinoma	Prospective case series	Follow-up period = 24 months	Ten patients (7 males, 3 females), age range: 65 - 89 years. LGD (n = 3), HGD (n =4), invasive carcinoma (n = 2) and carcinoma in situ (n = 1).	PDT using 5-ALA 30mg/kg orally followed by laser therapy 4 hours later, and limited to 2 treatments per patient. Patients were subsequently maintained on omeprazole 20mg daily to reduce acid reflux.	None	**Efficacy:** Columnar epithelial regression was seen in all patients with dysplasia (mean area decrease 44%; range 10-100%), with apparent elimination of dysplasia in all cases. In patients with in situ or invasive carcinoma, no response was seen. All patients were alive at 28 months **Adverse effects:** No serious side effects were observed. Mild chest pain (n =3), nausea lasting 24 hours (n= 1),	Subjects remained in hospital over-night, but were allowed home the next morning. Standard small case series

Study ID	Aim	Study design	Follow-up	Population	Intervention	Comparison	Outcome(s)	Comments
Ban; 2004	To evaluate the efficacy of PDT for dysplasia and early adenocarcinoma arising in BO	Retrospective case series (unselected consecutive patients)	Follow-up: 60 months	Thirty-three patients (mean age, 71 years) with HGD and/or intramucosal carcinoma but two patients had previously had distal oesophagectomy for invasive carcinoma and had developed recurrent HGD at the anastomosis	PDT ablative therapy using porfirmer sodium	None	**Efficacy:** Dysplasia and/or carcinoma were eradicated in 17 patients. Dysplasia and/or carcinoma persisted in 16 patients. Further analysis is done between the persistent and eradicated groups.	None

Study ID	Aim	Study design	Follow-up	Population	Intervention	Comparison	Outcome(s)	Comments
Barr; 1996	Eradication of high grade dysplasia (HGD) in columnar-lined BO by PDT with endogenously generated protoporphyrin	Prospective case series	Follow-up period = 26 - 44 months	Five patients (three males) with histologically confirmed HGD aged 56, 62, 74, 77, and 81. All had no evidence of invasive carcinoma on endoscopy, biopsy, and endoscopic ultrasound.	PDT with 5-ALA combined with long-term omeprazole (proton pump inhibitor) to eradicate high grade dysplastic columnar-lined oesophagus (BO).	None	**Efficacy:** HGD was eradicated in all patients and squamous regeneration occurred after acid suppression with a proton pump inhibitor. No patient has remaining HGD despite biopsy sampling. 2/5 patients had non-dysplastic Barrett's underneath regenerative squamous mucosa. **Adverse effects:** No complications or recurrence seen.	Small standard case series

Study ID	Aim	Study design	Follow-up	Population	Intervention	Comparison	Outcome(s)	Comments
Craig; 2007	To evaluate the efficacy of porfimer sodium PDT in the treatment of early oesophageal cancer.	Prospective case series	Mean length of follow-up was 30 months (range 2-56 months)	Total of 28 patients: 22/28 (78.6%) of patients had adenocarcinoma in situ of which 14/22 had associated Barrett's oesophagus. Median age was 74 years (range 61-90 years) with 66.6% male patients.	Ablation of early oesophageal cancer using porfimer sodium PDT.	None	**Efficacy:** 18/28 patients (64.3%) had a complete endoscopic and histological response to porfimer sodium PDT at between 6 and 8 weeks following therapy. 12/18 who had a complete response to treatment remained disease free for a median period of 1160 days (range 249-2019 days). Overall mortality was 6/8 giving a median survival of 750 days (range 54-2049 days) **Adverse effects:** Major complication was stricture formation (50%) requiring median dilations of 5 (1-31).. Most patients experienced minor short lived side effects of chest discomfort following initial PDT (no numbers given)	Standard case series, looking at complete response and survival.

Study ID	Aim	Study design	Follow-up	Population	Intervention	Comparison	Outcome(s)	Comments
Etienne; 2004	To evaluate the efficacy of photodynamic therapy (PDT) with green light and temoporfin or m-tetrahydroxyphenyl chlorin in patients with BO and early stage neoplastic lesion	Prospective case series	Mean follow-up was 34 months (range 12-68 months).	Twelve patients (11 men [mean age 70 years, range 56-81 years], one woman [age 76 years]) with BO with 14 lesions (7 HGD, 7 intramucosal adenocarcinoma) in these 12 patients were treated.	Ablative therapy with PDT using temoporfin or m-tetrahydroxyphenyl chlorin	None	**Efficacy:** Intramucosal adenocarcinoma and HGD were absent in biopsy specimens from all 14 treatment zones in the 12 patients (100% efficacy). Squamous re-epithelialisation was complete. A total of twenty PDT sessions were required to eradicate all 14 lesions **Adverse effects:** chest pain corresponding to the treatment area, 3 patients experienced bouts of hiccups arising several hours after PDT, asymptomatic bilateral pleural effusion was found in one patient, moderate fever was noted in 4 patients from 2-8 days after treatment and oesophageal stricture in one patient, and one photosensitivity reaction. Three deaths occurred that were unrelated to the lesions	Standard case series

Study ID	Aim	Study design	Follow-up	Population	Intervention	Comparison	Outcome(s)	Comments
Filonenko ; 2008	To evaluate the efficacy of PDT of early oesophageal cancer	Prospective case series	Follow-up period was 3-11 years	T1N0M0 Stage of 48 patients. Thirty-two patients were men and 16 women. Age range: 41-89, average age was 68. The greater part of patients (75.1%) was over 60. HGD and/or squamous cell carcinoma within mucous and submucous layers of oesophageal wall was in 34 patients (70.8%), adenocarcinoma with mucous and submucous invasion (early Barrett's oesophagus) was in eight (16.7%)	Ablation with PDT using Photogem, Photosens, Radachlorin, Alasens.	None	**Efficacy:** Complete regression in 37 cases (77%) of cancer (defined as complete tumour ablation), partial regression in 11 (23%) cases of cancer (defined as 50% tumour ablation. Median of survival: 4.59 years of oesophageal cancer patient. **Adverse effects:** Serious complications were not registered. Main complication was a temporary increase of skin photosensitivity that all patient had. A scar deformation of the oesophageal lumen in one patient.	Standard case series but with long term follow up

Study ID	Aim	Study design	Follow-up	Population	Intervention	Comparison	Outcome(s)	Comments
Foroulis; 2009	To evaluate the effectiveness of PDT in ablating HGD and/or intramucosal adenocarcinoma (IMC) complicating Barrett's oesophagus (BO).	Retrospective case series	Median post - PDT follow-up was 14 months (4-70) months	Thirty-one patients (20 male, 11 female). Mean age was 73.45 ± 9.38 years (range: 53-85 years, age > 80 years: 9 patients). HGD (n = 15), HGD and IMC (n = 10) and T1b or limited T2 adenocarcinoma in 6 patients	Ablative therapy with PDT using porfirmer sodium	None	**Efficacy:** Initial complete response to PDT was observed in 80.95% of patients with HGD/IMC. Partial response (no endoscopic abnormality, residual IMC-HGD on biopsy) in 9.52%. No response in 9.52%, but permanent complete response 71.42%, progression to adenocarcinoma 19.04% **Adverse Effects:** Symptomatic oesophagitis 16.12%; photosensitivity 12.9%; oesophageal stricture 6.45%, epigastric pain and nausea 3.22%	Standard case series

Study ID	Aim	Study design	Follow-up	Population	Intervention	Comparison	Outcome(s)	Comments
Gill; 2009	Effectiveness of PDT using Porfimer sodium photosensitizer in BO with HGD or mucosal cancer but also a dosimetry study.	Case series	6 – 12 weeks	Eleven patients. Age range: 53 - 83 years. Barrett's length: 1 - 15 cm	Ablative therapy with PDT using porfimer sodium	None	**Efficacy**: Six patients had complete ablation of Barrett's mucosa or carcinoma; five of these had no evidence of squamous or subsquamous abnormalities on follow-up endoscopy. Five other patients had residual Barrett's dysplasia or carcinoma. Therefore 5/11 with complete ablation. **Adverse effects:** One patient was found to have an oesophageal stricture.	Standard case series with varying dosimetry

Study ID	Aim	Study design	Follow-up	Population	Intervention	Comparison	Outcome(s)	Comments
Gossner; 1998	Safety and efficacy of PDT on HGD and early cancer in BO by means of 5 - Aminolevulinic Acid	Prospective case series	Follow-up lasted 1-30 months	Thirty-two patients (8 women and 24 men; age, 41-88 years; mean age, 68.5 years). HGD (N = 10). Early adenocarcinoma (n = 22)	Ablative therapy using PDT by means of 5 - ALA	None	**Efficacy:** All patients with severe dysplasia had normal endoscopic ultrasound findings. Patients with early mucosal cancer, a normal oesophageal wall or tumour of ≤2mm was found in 17 of 22 cases. Complete remission achieved in 10 of 10 patients with HGD (100%). Complete remission in 17 of 22 patients with early carcinoma (77%). Therefore overall 84.4%. **Adverse effects:** fifteen patients experienced transient nausea up to 6 hours after PDT. No patient had severe side effects, including phototoxicity.	Standard case series with further biological markers also analysed

Study ID	Aim	Study design	Follow-up	Population	Intervention	Comparison	Outcome(s)	Comments
Gossner; 1999	To demonstrate the safety and efficacy of a new long-range through the scope balloon applicator for photodynamic therapy in BO	Prospective case series	12 months (range 10-15 months)	Six patients (two women and four men, aged 48 - 79). Severe dysplasia HGD (n = 2), early adenocarcinoma (n = 2), or superficial squamous-cell carcinoma of the oesophagus (n = 2) (uT1 N0 M0 on endoscopic ultrasound).	Ablative therapy using PDT by means a new long-range through the scope balloon applicator using 5 - Aminolevulinic Acid or intravenous administration of meta-(tetrahydroxyphenyl)chlorine	None	**Efficacy:** HGD was eradicated in all patients (2/2) and two of the cancer patients had cancer eradication (2/4) after an average of 1.3 treatment sessions. **Adverse Effects:** No treatment-related mortality or morbidity was observed in terms of major side effects such as strictures formation or perforation	Standard case series

Study ID	Aim	Study design	Follow-up	Population	Intervention	Comparison	Outcome(s)	Comments
Javaid; 2002	Efficacy of PDT using oesophageal dysplasia and early carcinoma in BO.	Prospective case series	Follow-up was 12.8 months (4-27) months	Seven consecutive patients treated with PDT in an open non-randomised trial. HGD (n = 6), superficial oesophageal carcinoma (n = 1). Age range: 49 - 84 years with a mean age of 68years. Five of the seven patients were male. The mean length of the Barrett's segment was 6.6cm (range 1.2-13 cm)	Ablation of BO with HGD and early oesophageal cancer with PDT using meta-(tetrahydroxyphenyl)chlorine	None	**Efficacy:** Dysplasia was eradicated in all patients. **Adverse effects:** Oesophageal strictures (n = 2).	Standard case series

Study ID	Aim	Study design	Follow-up	Population	Intervention	Comparison	Outcome(s)	Comments
Keeley; 2007	To evaluate the safety and efficacy of PDT in BO with HGD and superficial oesophageal cancer	Retrospective case series	Mean follow-up of 28.1 months, ranged from 1 month to almost 7 years (81 months)	Fifty patients underwent PDT. There were 37 males and 13 females. Age range: 41 - 88 years old (mean age 74.4). Thirteen patients (26%) had Barrett's HGD, 6 (12%) had small intramural carcinomas, 16 (32%) had T1 N0 tumours.	PDT with the curative intent using Photofrin	None	**Efficacy:** Five of the 13 HGD patients (38%), treated with curative intent, show no evidence of recurrence during follow-up after an average of 1.4 PDT sessions. **Adverse effects:** Stricture formation occurred in 21 patients (42%), sunburn (photosensitive reaction) ([n =2] 4%), and pleural effusion ([n = 3] 6%)	Standard case series

Study ID	Aim	Study design	Follow-up	Population	Intervention	Comparison	Outcome(s)	Comments
Laukka; 1995	To treat BO with low-dose PDT with hematoporphyrin derivative (HpD).	Prospective case series	One year period of follow-up.	Five patients consisting of 4 men and one woman with a median age of 69 years (range 56 to 80 years).	PDT of BO with low-dose hematoporphyrin derivative (HpD). All study subjects were supplied with omeprazole 20mg orally each day for the first 6 months.	None	**Efficacy:** A decrease in the length of columnar epithelium was found in five patients with a mean reduction of 2.4 ± 0.9cm (range 1 to 5). Representing a mean decrease in overall length (range 10% to 50%). **Adverse effects:** nausea, epigastric pain, and anorexia (n = 2) lasting 1 to 5 days following PDT and mild erythema (n = 2)	Standard case series

Study ID	Aim	Study design	Follow-up	Population	Intervention	Comparison	Outcome(s)	Comments
Lovat; 2005	To evaluate the efficacy and complications of m-tetrahydroxyphenyl chlorin (mTHPC) PDT.	Prospective case series	The mean length follow-up was 24 months (1-72 months).	Nineteen consecutive patients (7 with HGD, 12 with early adenocarcinoma) were treated. Sixteen males and 3 females. Age range: 40 - 81 years.	Ablative PDT therapy using m-tetrahydroxyphenyl chlorin (mTHPC)	None	**Efficacy:** Four out of six patients (4/6) with cancer and 3/4 with HGD were successfully ablated with PDT. Buried Barrett's under regenerated squamous epithelium was found in 4 patients. **Adverse effects:** Fatal aortoesophageal fistula in one patient (one procedure related death), stricture in another patients and skin photosensitivity in 2 patients.	Study also looks at effect of green versus red light on PDT ablation.

Study ID	Aim	Study design	Follow-up	Population	Intervention	Comparison	Outcome(s)	Comments
Mackenzie; 2008	This is a non-randomised light dose escalation study to evaluate the effectiveness of PDT in ablating HGD in Barrett's oesophagus (BO)	Prospective case series	Median follow-up was for 45 months (1-78 months).	Twenty-four patients with HGD (19 men, 5 women) were recruited. Median age at treatment was 73 years (range 52-87 years). Median length of Barrett's mucosa was 6cm (range 1-12).	PDT with 5-ALA for ablation of high grade dysplasia in Barrett's oesophagus (BO).	None	**Efficacy:** Six out of eight patients (75%) treated with the highest light dose (1000J/cm x2) compared to one out of two (50%) with a single high light dose treatment, two out of nine (22%) receiving medium light dose, and zero out of five (0%) receiving low light dose had successful long-term eradication of HGD. Reduction of the length of Barrett's. Two patients had complete ablation of their Barrett's segment. **Adverse effects:** No skin photosensitivity reactions and no oesophageal strictures developed. Nausea and vomiting occurred in two thirds of patients, chest discomfort, and elevation of Alalnine transaminase (ALT), one patient developed aspiration pneumonia.	Standard case series but studying effect of light dose on PDT ablation

Study ID	Aim	Study design	Follow-up	Population	Intervention	Comparison	Outcome(s)	Comments
Mino-kenudson ; 2007	To evaluate the prevalence, endoscopic and histologic characteristics and also response to further treatment of buried neoplastic epithelium after PDT	Prospe ctive case series	Follow-up: seven years.	Total of 52 consecutive patients: HGD n=19 and intramucosal adenocarcinoma n=28 and invasive adenocarcinoma n=5. Forty men and 12 women with a mean age of 72.2 years (range: 45 to 94). Forty-eight patients (92%) had long segment BE (<3cm).	PDT using Porfimer sodium	None	**Efficacy:** At the end of follow-up, BO was eradicated in 32 patients (61.5%). Neoplastic lesions were eradicated in 40 patients (76.9%) and persisted or recurred in 12. among the persistent group, the diagnosis was downgraded in 2 patients (HGD to LGD: 1; IMC to LGD: 1). **Adverse effects:** Not studied	Standard case series but looking at several irrelevant outcomes

Study ID	Aim	Study design	Follow-up	Population	Intervention	Comparison	Outcome(s)	Comments
Overholt; 1999	To study clinical efficacy of PDT in Barrett's oesophagus.	Case series	mean 19 months (4-84 months)	100: with 13 superficial cancers, but efficacy available for 85 (T1=12; HGD=73) patients	using 2 mg/kg porfirmer sodium 2 days prior to PDT, 400mW/cm; 100-250J/cm; + OM 20mg/ two times a day for first 3 months and then once/day	None	**Efficacy:** Complete eradication of Dysplasia CR-D - T1 8/12 and HGD 56/73; overall - 64/85 Complete Barrett's eradication - T1 4/12 and HGD 32/73 : overall - 36/85 **Adverse effects**: Stricture: 34/100; Photosensitivity: 4/100; atrial fibrillation: 3/50	Study looking at ablation of dysplasia/ Barrett's; Porfimer sodium PDT. Standard single centre case series.
Overholt, 2003	To study clinical efficacy of PDT in Barrett's oesophagus.	Case series	Mean 50.7 months (SD 20.7), (range2-122 months) long term survival analysis	103: high grade dysplastic Barrett's or early adenocarcinoma HGD=80 and CA=9	using 2 mg/kg Porfimer sodium 2 days prior to PDT, 400mW/cm; 100-250J/cm; + OM 20mg/ two times a day for first 3 months and then once/day	None	**Efficacy:** HGD - Complete eradication of Dysplasia and Barrett's - 43/80 (53.8%); eradication of Dysplasia but persistence of Barrett's 19/80 (23.8%); HGD2/80; progression to cancer 1/80; Death 7/80 CA GP- Complete eradication of cancer, Dysplasia and Barrett's - 3/9 (33.3%); eradication of dysplasia but persistence of Barrett's 1/9 (11.1%); death 5/9 (55.6%) OVERALL IIT success survival rate was 77.5% HGD and 44.4% CA. Overall ablation was achieved 1-3 courses of PDT **Adverse effects:** Stricture: 30% overall; 18% for 1 PDT and 50% for 2 PDT courses. The figures for	Good long term follow-up using ITT; survival analysis using Kaplan Meier curves.

Study ID	Aim	Study design	Follow-up	Population	Intervention	Comparison	Outcome(s)	Comments
							adverse effects remain the same as 1999 (Stricture: 34/100; Photosensitivity: 4/100; atrial fibrillation: 3/50). In addition small unilateral or bilateral pleural effusions were seen in majority of patients but two patients required thoracentesis.	
Overholt, 2005, 5007	To compare the clinical efficacy of PDT+ omeprazole versus omeprazole alone	RCT	Median 59 ± 2.7 months for the PDT group and 61 ± 5.8 months for surgery	208; 138 PDT vs 70 Omeprozole (OM) alone, all HGD Barrett's	PDT VS Omeprozole PDT using 2 mg/kg porfirmer sodium vs. 20mg OM twice a day	PPI (omeprazole)	**Efficacy:** Complete absence of high grade dysplasia CR-HGD- PDT 106/138 (77%) vs. OM 27/70 (39%); Complete eradication of Dysplasia CR-D - PDT 81/138 (59%) vs. OM 10/70 (14%); Progression of dysplasia/ disease to cancer - PDT21/138 (15%) vs. OM20/70 (29%); squamous overgrowth pre and post treatment: PDT 8/138 to 39/132 vs. OM 2/70 to 22/67 **Adverse effects:** In PDT arm: Photosensitivity 69%; Stricture 36%; Nausea 11%; chest pain 20%; none for OM alone arm	This is a partially blinded randomised phase III trial, 30 international centres that used 90% power to detect a CR-HGD of 27-60% with a significance of 0.05 but recruited 208 patients instead of required 117 to allow for drop outs. They used the IIT principle for

Study ID	Aim	Study design	Follow-up	Population	Intervention	Comparison	Outcome(s)	Comments
								analysis. Clear exclusion and inclusion criteria, appropriate primary and secondary outcomes, good explanation of techniques - 2 further papers with longer follow up time and molecular outcomes. The further follow up sustained the statistical significant improvement in the PDT arm and no serious AES occurred in the 2yr -5 yr period.

Study ID	Aim	Study design	Follow-up	Population	Intervention	Comparison	Outcome(s)	Comments
Pech; 2005	To evaluate the efficacy Of Aminolaevulinic Acid-induced Photodynamic therapy (ALA-PDT) and the survival of patients with early Barrett's neoplasia.	Prospective case series	Median follow-up period of 37 months (interquartile range 23-55)	sixty-six patients (mean [standard deviation] age 61.4 [10.2] years) with high-grade intra-epithelial neoplasia ([HGIN] group A; n = 35) and early adenocarcinoma (group B; n = 31)	ALA-PDT was carried out in 66 patients with HGIN and mucosal adenocarcinoma in Barrett's oesophagus.	None	**Efficacy:** A total of 34 of the 35 patients in group A (97%) and all patients in group B (100%) achieved a complete response. One local recurrence was observed in group A and 10 in group B ($p < 0.005$). Disease free survival in patients with HGIN was 89%, and in patients with mucosal cancer, it was 68%. The calculated 5-year survival was 97% in group A and 80% in Group B. The patients received 1-3 PDT treatments. **Adverse effects:** No major complication was observed. 7 deaths occurred but they were not procedure or tumour related. Minor complications of nausea, vomiting and chest pain occurred in 40% of the patients.	Long term study follow-up with survival analysis. The article states that patients reported in previous publications were not included for this study.

Study ID	Aim	Study design	Follow-up	Population	Intervention	Comparison	Outcome(s)	Comments
Prasad, 2007a	To compare efficacy of ablation of surgery and PDT	retrospective cohort	Median 59 ± 2.7 months for the PDT group and 61 ± 5.8 months for surgery	199: 129 PDT vs. 70 oesophagectomy	26 patients - hematoporphyrin derivative (94mg/kg) ; 103 patients Porfimer sodium (2 mg/kg); 48 hrs prior to PDT	Surgery	**Efficacy:** Overall mortality: PDT=11/129 vs surgical 6/70 NS (Wilcoxon test = 0.0924; P = 0.76). HGD eliminated in 88% of PDT in 1 year and 86% by 3 year follow up. **Adverse effects:** Uses AES for PDT from earlier study 131 patients. For surgical group; median length of stay=11 days; 9 were readmitted within 90 days and 9 patients developed strictures	Good long term true cohort study using ITT; survival analysis using Kaplan Meier curves, PDT versus surgery. Baseline comparison of characteristics was controlled for in survival analysis.
Prasad 2007b	To study the predictors for stricture from PDT	retrospective case series	not stated	131consecutive patients: all with HGD (162 PDT courses)	26 patients - hematoporphyrin derivative (94mg/kg) ; 105 patients Porfimer sodium (2 mg/kg); 48 hrs prior to 200J/cm fibre	None	The minimum number of dilations required for sustained relief was 4, for median of 12 weeks (1-104 weeks). History of prior oesophageal stricture (OR=2.73, 95%CI=1.15-6.47); ER prior to PDT (OR=2.72, 95%CI=1.13-6.59); No. of PDT applications (OR=2.24, 95%CI=1.22-4.12); prior ER was not significant in univariate analysis; Stricture: 35/131 (27%) = 23% using porfirmer sodium vs. 25% using hematoporphyrin derivative (NS, P>0.1)	Stricture was defined as symptomatic dysphagia; Single centre retrospective cohort study looking at predictors for stricture.

Study ID	Aim	Study design	Follow-up	Population	Intervention	Comparison	Outcome(s)	Comments
Weiss; 2006	To determine if Photodynamic therapy (PDT) is an alternative to oesophagectomy in BE patients with high grade dysplasia (HGD) or early cancer.	Prospective case series	Mean follow up time was 21 months, with a range of 3 – 55 months	Seventeen patients (15 men, two women; mean age 74.6 years, range 52 to 96 years). Thirteen of the 17 patients had HGD and four had early oesophageal adenocarcinoma.	PDT using Porfimer sodium.	None	**Efficacy:** After PDT, HGD or early cancer was eliminated in 9/15 (60%) patients. Barrett's mucosa was completely eliminated in four patients. **Adverse effects:** 2 photosensitive reactions, pleural effusions=2, strictures =1 and atrial fibrillation=1.	Standard case series
Wolfsen; 2002	Evaluating results using PDT for the treatment of dysplasia or superficial cancer in patients with BO.	Retrospective case series	Mean follow-up time: 18.5 (range, 1-56) months	Forty-eight patients with BO and HGD (34 patients) or superficial oesophageal cancer (14 patients).	PDT (non-balloon system) using Porfimer sodium for Barrett's oesophagus. All patients were treated with 40-80 mg omeprazole twice daily.	None	**Efficacy:** Twenty seven patients (56%) experienced complete ablation of Barrett epithelium after PDT. **Adverse effects:** Stricture in 11 patients, photo-sensitivity reactions in 7 patients, atrial fibrillation in 1 patient, and recurrent congestive heart failure in 1 patient.	Standard case series but with survival analysis done using Kaplan Meier curves

Study ID	Aim	Study design	Follow-up	Population	Intervention	Comparison	Outcome(s)	Comments
Wolfsen, 2004a	Study looking at factors that may affect complete ablation of Barrett's	Case series	median 1.6 years (0.5-6.5 years)	Total of 102: 69 HGD and 33 mucosal adenocarcinoma, confirmed by contrast enhanced computerized tomography (CT) and endoscopic ultrasound	PDT using 2 mg/kg Porfimer sodium intravenously + Outpatient endoscopy with solid state diode laser 48h/ 72hours + 80-120 mg/day OM or esomeprazole	None	**Efficacy:** All had 1 course of PDT: Barrett's eradication/ Ablation **-** 57/102 (56%); No difference in ablation between genders/ BHDGVS Carcinoma/ Newly diagnosed vs. established surveillance; but BO length was significantly shorter in HGD vs. carcinoma (5 cm vs. 3 cm; p<0.001). Only 29/67 (62%) patients where dysplasia or carcinoma was detected in initial endoscopy had oesophageal disease symptoms of chest pain/ dysphagia/ chronic gastro-oesophageal condition). **Adverse effects:** Stricture 20/102 (20%); Photosensitivity 18/102 (18%); chest pain 15/102 (15%); cardiac complication 2/102 (2%); dysphagia in 11/102 (11%); oesophageal perforation in 1/102 patients (1%)	One centre study looking at factors that may affect complete ablation for BO. Standard case series

Study ID	Aim	Study design	Follow-up	Population	Intervention	Comparison	Outcome(s)	Comments
Yachimski, 2008	Study looking at predictors for stricture	retrospective case series	minimum of 3 months for inclusion	116: HGD+IMC+ T1 (160 courses of PDT), mixed population of high-grade dysplastic BO, intramucosal cancer and early adenocarcinoma	PDT with Photofrin 2mg/kg (except till 1998 cap of 150mg was kept) + OM 40mg/ two times a day prior to PDT and indefinitely after PDT	None	**Efficacy:** 116 patients had 160 courses of PDT (79 = 1 course; 31=2 courses; 5=3 courses and 1=4 courses). Majority had maximum light dose of 150J/cm. The predictors of stricture that were statistically significant were: length of BO (OR=1.27; 95%CI=1.04-1.44); multiple PDT courses (OR=3.15; 95%CI=1.43-6.94) and presence of intramucosal or sub mucosal carcinoma pre-treatment (OR=4.62; 95%CI=1.66-12.89). No association with prior ER **Adverse effects:** Only looked at Stricture rate overall based on number of courses = 37/160 (23%) or based on first/ index course = 19/116 (16%)	Study looking at predictors for stricture (using data from a single large urban teaching hospital), univariate and a multivariate logistic regression analysis was undertaken; considered many predictors/ variables associated with the treatment and patients. Majority of strictures occur within 3 weeks of treatment so maximum follow - up may not be essential.

Study ID	Aim	Study design	Follow-up	Population	Intervention	Comparison	Outcome(s)	Comments
Yachimski, 2009	To study the factors affecting complete ablation of Barrett's	retrospective case series	longer than 12 month follow-up	Total of 116: HGD+IMC+ T1 (160 courses of PDT); mixed population of high-grade dysplastic BO, intramucosal cancer and early adenocarcinoma	PDT with Photofrin 2mg/kg on day 0 followed by light (150J/cm) 630nm on days 2 and 4; for patients with residual non-dysplastic or LGD BO multipolar coagulation was offered. Another PDT course offered only if HGD or IMC	None	**Efficacy:** The patients had 1-4 courses of PDT. The use of multipolar coagulation to treat residual patches of Barrett's was done in 61/116; and was associated with successful eradication of HGD/ CA 60% vs. 34%p=0.01. Younger patients were more successful for CR-HGD/CA (69.5 yrs vs 72.5, P=0.04); CR-HGD/CA - 81/116 (70%); CR-BO 45/116 (39%); shorter length of BO was associated with higher complete ablation of BO (5.0±3.2cm vs 6.7±3.3cm, p=0.009); multivariate analysis showed multiple PDT courses, length of BO and multipolar coagulation significantly associated with successful ablation of BO but after Bonferroni correction at p=0.025 left only length of BO (>3 cm vs. <3 cm) significant at OR 0.15, 0.04-0.50 p=0.002)	Study looking at predictors for complete ablation of CR-HGD/CA and BO. Case series controlling for many variables in multivariate regression analysis, but is retrospective and has no control group for comparison

Table 9 Evidence Table for included ER+APC studies

Study ID	Aim	Study design	Follow- up	Population	Intervention	Comparison	Outcome(s)	Comments
Peters 2006	To prospectively evaluate safety and efficacy of stepwise radical endoscopic resection (ER) of Barrett's oesophagus containing early neoplasia	Prospective case series	median 11 months	n=39 but 37 for analysis; 2 discontinued due to co morbidity Early neoplasia (i.e., high-grade intraepithelial neoplasia or early cancer) in Barrett's length ≤5 cm, without signs of sub mucosal infiltration or lymph node/distant metastases	Analysis in 37 but ER and APC in 34/37	None	**Efficacy:** eradication of dysplasia/CA - 37/37; eradication of BO 33/37 **Adverse effects:** perforation1/37; bleeding 1/37; Stenosis 10/39	Patients were given APC after ER for residual BO ablation

Study ID	Aim	Study design	Follow- up	Population	Intervention	Comparison	Outcome(s)	Comments
Pouw 2008	To assess safety and efficacy of SRER in patients with Barrett's oesophagus with high-grade intraepithelial neoplasia (HGIN) or early cancer	Retrospective case series	median 23 months (15-41 months)	n=34 22 with HGIN 12 with early carcinoma Barrett's oesophagus with HGIN or early cancer	ER - stepwise radical APC done in 12	None	**Efficacy:** 23 has complete eradication of BO; recurrence of HGD/CA in 3- 2 had repeat ER and 1 surgery; recurrence of non-dysplastic BO in 5	Study for ER but APC was also done in 12 cases post ER

Table 10 Evidence Table for included ER+RFA studies

Study ID	Aim	Study design	Follow-up	Population	Intervention	Comparison	Outcome(s)	Comments
Beaumont; 2009	To evaluate the efficacy and safety of stepwise circumferential and focal RFA using the HALO system for Barrett's oesophagus containing flat, high-grade dysplasia (HGD) or residual dysplasia after endoscopic resection for HGD or intramuscular cancer (IMC)	Prospective case series	Not stated	Total of 22 participants: but only 12 patients with Barrett's with HGD, compared with 10 healthy volunteers	Stepwise circumferential and focal RFA	Oesophageal structure of patients with Barrett's after RFA was compared to asymptomatic participants. RFA was also compared to other techniques.	**Efficacy:** All patients had complete eradication of HGD and IMC after ablation. Also with complete endoscopic and histologic removal of all intestinal metaplasia. Baseline oesophageal diameter was unchanged by RFA. Median oesophageal diameter before and after treatment were 31.5mm and 31.3mm respectively (p = 0.87). LES resting pressure increased in patients with Barrett's from 4.0mmHg, IQR 2.0-5.0mmHg, p = 0.02 to 4.0mmHg, IQR 3.0-8.0mmHg, p = 0.02.	Comparison was based on literature reviews not on clinical trials. Small sample size

Study ID	Aim	Study design	Follow-up	Population	Intervention	Comparison	Outcome(s)	Comments
Gondrie; 2008a	To evaluate the efficacy and safety of stepwise circumferential and focal RFA using the HALO system for Barrett's oesophagus containing flat, high-grade dysplasia (HGD) or residual dysplasia after endoscopic resection for HGD or intramuscular cancer (IMC)	Prospective case series	14 months median follow up (IQR 13-15).	Twelve patients (nine men; median age 70 years [range, 53-76 years]) were treated (median Barrett's length 7cm [range 6.5-8]). Inclusion criteria:	Combined approach of endoscopic resection followed by stepwise circumferential and focal RFA	None	**Efficacy:** Complete remission of dysplasia was achieved in 12/12 patients (100%). Complete endoscopic and histological removal of Barrett's oesophagus was achieved in 12/12 patients (100%). **Adverse effects:** There were no ablated-related stenoses.	All ablation sessions were performed as outpatient procedures, there were no severe complications. Limitations: Observer bias (pathologist). Instrument bias. Data obtained in cases of prior endoscopic resection might not be correct.

Study ID	Aim	Study design	Follow-up	Population	Intervention	Comparison	Outcome(s)	Comments
Gondrie: 2008b	To evaluate the efficacy and safety of stepwise circumferential and focal RFA using the HALO system for Barrett's oesophagus after endoscopic resection for visible lesions	Prospective case series	Patients were followed up for a median period of 19 months (IQR 18-22) after the first ablation session and 14 months (IQR 9-14) after achieving complete endoscopic removal of all BO.	Eleven patients (eight men; median age 60years) were treated. LGD (n = 2) and HGD (n = 9). Mean Barrett's length 5cm.	Stepwise circumferential and focal RFA of Barrett's oesophagus with HGD.	None	**Efficacy:** Complete remission of dysplasia and complete endoscopic and histological removal of Barrett's oesophagus was achieved in 11/11 patients (100%). None of these patients showed recurrence of dysplasia. **Adverse effects**: There were no severe complications.	All ablation treatment sessions were carried out as outpatient procedures.

Study ID	Aim	Study design	Follow-up	Population	Intervention	Comparison	Outcome(s)	Comments
Pouw; 2009; 2010	Assessing the safety and effectiveness of RFA for treating Barrett's oesophagus containing High Grade Intraepithelial Neoplasia (HGIN) and/or early cancer	Prospective single arm cohort	Median follow-up time of 22 (IQR 17.2-23.8) months.	All had HGIN and/or early cancer. Patients; N=24	Circumferential and focal RFA after endoscopic resection	None.	**Efficacy:** Complete eradication of endoscopic intestinal metaplasia was seen in 20/24 (83.3%) and complete eradication of neoplasia in all patients. Of the 23 patients who were approached for biopsy depth and BGM evaluation, all post-RFA biopsies from the NSE contained full epithelia, whereas 37% contained lamina propria, a finding no different from biopsies from untreated squamous epithelium (36% lamina propria).	Small single arm observational study but with two publications relating to biological markers and clinical outcomes. The data was taken from three tertiary care medical centres in Europe.

Study ID	Aim	Study design	Follow-up	Population	Intervention	Comparison	Outcome(s)	Comments
Sharma; 2009	To assess the safety and efficacy of a stepwise regimen of circumferential and focal ablation using the HALO system for the treatment of BE with dysplasia.	Prospective Cohort	Follow-up was for 62 out of 63 patients (median 24 months).	24: A total of 63 patients were treated (57 men; median age 71 years; median BE length 5cm), Low Grade Dysplasia (LGD) [n = 39] and High Grade Dysplasia (HGD) [N = 24]. All nodular diseases at baseline or during follow-up were endoscopically resected.	RFA therapy using the HALO system plus surveillance. All patients received a high-dose regimen of proton pump inhibitor (esomeprazole 40mg bid) until eradication of all intestinal metaplasia (IM) was documented.	Efficacy of treatment between the LGD cohort and the HGD cohort	**Efficacy:** A complete response (CR) is defined as all biopsies negative for intestinal metaplasia (IM) (CR-IM) or dysplasia (CR-D) at last available follow-up. For the HGD cohort: 67%CR-IM, 79%CR-D and 100%CR-HGD. There were no buried glands in > 1,000 biopsies.	Cohort study but with only one arm and no control group.

Study ID	Aim	Study design	Follow-up	Population	Intervention	Comparison	Outcome(s)	Comments
Smith; 2006	To determine the optimal treatment parameters for the ablation of intestinal metaplasia (IM) containing high grade dysplasia (HGD) using a balloon-based RFA	prospective Case series	12-18 months	Eight patients with a mean age of 57 years (range, 45-71 years) were enrolled and treated. All patients had a documented histopathologic diagnosis of IM-HGD (mean length, 7cm; range, 4-10cm).	Patients underwent ablation of circumferential segments of the oesophagus containing IM-HGD using the HALO^{360} system (RFA). The treatment settings were randomized to 10, 12, or 14J/cm² for two, three, or four applications.	None	**Efficacy:** The mean ablation component time was 16 min (range, 1-45 min) Complete removal or ablation of all IM and HGD was achieved in 9 of 10 ablation zones. The maximum ablation depth was the lamina propria or muscularis mucosae. The highest energy (14J/cm², 4 applications) incurred edema in the superficial submucosa, but no submucosa ablation. **Adverse effects** There were no device-related adverse events.	The maximum ablation depth increased as the combination of energy density and number of application escalated. With an increase from 10 to 14 J/cm², and from two to four applications, the depth of ablation moves generally from the lamina propria to the muscularis mucosae, or from a partial muscularis mucosae ablation to a muscularis mucosae ablation with submucosa edema (at the highest treatment combination).

Table 11 Evidence Table for included ER+PDT studies

Study ID	Aim	Study design	Follow- up	Population	Intervention	Comparison	Outcome(s)	Comments
Behrens 2005	Studying the efficacy and safety of local endotherpies (ER+PDT)	Prospective case series	36 months (7-61 months)	N=44; Patients with HGD	ER + PDT (using 5-ALA). 14 patients had ER alone and 27 PDT and 3 had a combination, but all results reported together One patient in the ER group also received APC treatment	None	**Efficacy:** Range of 1-4 sessions to get 43/44 complete local remission (no neoplasia) and 39/44 complete ablation	Standard case series

Study ID	Aim	Study design	Follow- up	Population	Intervention	Comparison	Outcome(s)	Comments
Buttar 2001	To study the efficacy of combining ER and PDT	Prospective case series	median 13 months	N=17; T_1 or T_0 cancers with Barrett's origin	ER and PDT using porphyrin based photosensitisers	None	12 patients required 1 PDT session, 3 patients received additional photo radiation after 24 hours of initial treatment due to presence of small, non-necrotic mucosal islands. 2 other patients required 2 and3 sessions of PDT **Efficacy:** Complete ablation 16 (94.11%); Complete eradication of dysplasia in 14.17 (82%) patients **Adverse effects**: bleeding 1 (5.88%); stricture 5 (29.41%); photosensitivity 2 (11.76%); cardiac complication 1 (5.88%)	Standard case series

Study ID	Aim	Study design	Follow- up	Population	Intervention	Comparison	Outcome(s)	Comments
Mino-Kenudson 2005	To report experience with emphasis on diagnosis, staging, and therapeutic efficacy	Case series	mean 28 months for ER+PDT; 41 months for post-ER	N=18 with 27 ER. Three patients also had PDT prior to ER and follow up data available for 17 patients of whom 12 had PDT post ER. Barrett's oesophagus from LGD to invasive: 22/27 relevant lesions: 14 IMC, 8 HGD, (2 LGD and 3 advanced cancer)	ER and PDT	ER alone	**Efficacy:** Complete ablation ER+PDT 7/ 12 (58.3%)	Study with limited clinical outcomes and focus on correct staging and diagnosis
Van Hillegersberg 2003	Studying ablation using ER and PDT	Prospective case series	12 and 15 months	N=2; Patients with early cancer for BO	ER and PDT (using 5-ALA)	None	**Efficacy:** 1 failure persistence of HGD, 1 had no cancer residual post treatment.	Series of 2 case reports

Study ID	Aim	Study design	Follow- up	Population	Intervention	Comparison	Outcome(s)	Comments
Wolfsen 2004b	Using ER followed by PDT for staging and ablation	Prospective case series	median 13 months (6-46 months)	N=3; Patients with HGD for BO	ER and PDT (using porfimer sodium)	None	**Efficacy:** Complete ablation of BO in all	Small study looking at both staging and ablation