Original research

Oncological impact of universal endoscopic submucosal dissection for large Barrett's cancers

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ABSTRACT

Background Oncological principles favour en bloc R0 excision for curative endoscopic resection. In Barrett's neoplasia, endoscopically curable cancers include T1a and selected early T1b disease. Although endoscopic mucosal resection (EMR) and endoscopic submucosal dissection (ESD) are established treatments, optimal lesion selection remains debated.

Objective To evaluate the oncological impact of two selective resection strategies: (1) prioritising ESD for suspected Barrett's cancers >15 mm and (2) a historical approach reserving ESD mainly for advanced cancers.

Design Multicentre retrospective observational study comparing an ESD-first strategy (period 2, 2017–2024) with a historical selective ESD approach (period 1, 2004–2016). Lesion allocation was based on endoscopic assessment of invasion in both periods. Outcomes included basal R0 resection, curative resection, recurrence and adverse events.

Results A total of 581 resections were performed in 542 patients (median lesion size 20 mm). Cancer was present in 271 cases (178 T1a and 93 T1b). Period 2 had a higher cancer burden (52.3% vs 34.9%) and greater ESD use (77.1% vs 21.2%). Basal R0 resection improved from 69.7% to 91.2% (p<0.001), with the greatest benefit in T1b lesions (33.3% to 81.9%, p<0.001). In T1b cancers, curative resection increased (9.5% to 30.5%, p=0.043) and recurrence decreased (55.6% to 23.6%, p=0.043). ESD achieved higher 2-year cancer-free survival than EMR (87.4% vs 50%, p=0.021). Adverse events were infrequent (2.2%) and similar between techniques.

Conclusion Prioritising ESD for Barrett's cancers >15 mm improves basal R0 resection, reduces recurrence and improves short-term survival for T1b disease, supporting routine ESD for all larger Barrett's cancers.

INTRODUCTION

Barrett's-related early oesophageal adenocarcinoma is confined to the mucosa (T1a) or submucosa (T1b) and accounts for approximately 20% of all diagnosed cases.[1] Although oesophagectomy has been the standard treatment, providing up to 90% 5-year survival for T1a disease,[2] it is associated with significant risks, including 30-day mortality in 2–10% and up to 50% long-term morbidity, even in high-volume centres.[3]

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Endoscopic resection offers curative potential for early Barrett's-related oesophageal adenocarcinoma. However, the optimal selection between endoscopic mucosal resection (EMR) and endoscopic submucosal dissection (ESD) remains unclear due to diagnostic limitations and subjective guideline criteria.

WHAT THIS STUDY ADDS

⇒ A selective resection algorithm based on all suspected Barrett's cancers >15 mm yields excellent basal R0 rates for both T1a and T1b cancers and is superior to limiting ESD only for suspected advanced cancers.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ This algorithm optimises oncological outcomes, avoids piecemeal resection of cancers, preserves EMR for non-cancerous lesions and may inform guideline updates while improving treatment planning in expert endoscopic centres.

Recent studies have shown that endoscopic resection for T1a disease can yield long-term outcomes comparable to those of surgical resection.[3–7] In the absence of high-risk features, including poor differentiation and lymphovascular invasion, T1a disease has a 1–2% risk of lymph node metastasis, making complete endoscopic excision potentially curative. T1b disease was initially thought to have a high lymph node metastasis rate (12–50%) based on surgical pathology case series, leading to oesophagectomy being the treatment of choice for fit patients. However, contemporary data suggest that low-risk T1b disease, defined as submucosal invasion less than 500 µm deep from the muscularis mucosae (SM1) and without high-risk features, has a lymph node metastasis rate of approximately 4% and may also be cured with endoscopic resection.[8] Furthermore, there is emerging evidence to suggest that high-risk T1a/T1b disease that has undergone an endoscopic R0 excision (clear margins) may be amenable to endoscopic surveillance due to the low risk of subsequent lymph node metastasis.[8 9]

Oncological principles typically advocate for en bloc, R0 excision of all cancers to facilitate a cure and mitigate the risk of recurrence. However, for low-risk T1a disease, piecemeal endoscopic mucosal resection (EMR) is considered an acceptable approach.[10 11] This is because basal margins are generally cleared as the plane of resection is typically within the submucosal layer, while horizontal margins can be addressed with multiple resections.[12] Comparatively, for T1b disease, endoscopic submucosal dissection (ESD) is preferred, as it allows for R0 excision at the level of the muscularis propria. ESD also informs complete T staging and subsequent treatment decisions and does not preclude or compromise subsequent surgery if advanced tumour biology is detected within the resected specimen.[13–16]

Given these considerations, pre-resection knowledge of the T-stage and tumour biology, such as lymphovascular invasion and differentiation status, could guide the decision between EMR and ESD. However, current diagnostic tools, including biopsies and endoscopic ultrasound examination are inaccurate, and endoscopists are also unable to optically differentiate between T1a and T1b disease.[17 18] While several studies have reported outcomes for endoscopic resection techniques in oesophageal adenocarcinoma, no clear framework exists for selecting the appropriate approach.[19–22] Existing guidelines remain subjective, recommending ESD for 'malignant' or 'bulky' lesions.[10 11] To address this gap, we conducted a multicentre prospective observational study to evaluate the effectiveness of our selective resection algorithm for Barrett's neoplasia, which aims to obtain an R0 excision of all T1a and T1b cancers.

PATIENTS AND METHODS

Study design, lesion assessment and selective resection algorithm

We conducted a retrospective observational study evaluating two sequential selective resection algorithms for Barrett's neoplasia. The same algorithm was applied concurrently in two tertiary referral centres in Australia and Belgium during period 1, and a revised algorithm was introduced and co-adopted at both centres during period 2.

During period 1 (January 2004 to December 2016), ESD was reserved for lesions with endoscopic features suggestive of deep submucosal invasion, when EMR was considered unlikely to be technically feasible. In practice, this included lesions with one or some of the following features: Rigid on endoscopic palpation, friable with spontaneous bleeding, nodular (Paris Is) or demonstrated significant ulceration that failed to heal with proton pump inhibitor therapy. Lesions without these features were preferentially managed with EMR.

In period 2 (January 2017 to April 2024), en bloc resection was prioritised to optimise oncological accuracy. ESD was selected for lesions with suspected ≥T1a disease, defined by biopsy proven cancer or optical features consistent with malignancy, when lesion size was >15 mm (figure 1). When ≥T1a disease was suspected but lesion size was ≤15 mm, EMR was performed, reflecting the recognised upper size limit for reliable en bloc EMR (figure 2).[12] Suspicion of ≥T1a disease was based on depressed (Paris IIc) or nodular (Paris Is) morphology, ulceration despite proton pump inhibitor therapy or disrupted pit and microvascular patterns on high-definition or magnification endoscopy.

The indication for ESD evolved from a depth-driven rescue strategy in period 1 to a proactive en bloc oncological strategy in period 2, with lesion size used to triage between ESD and EMR once cancer was suspected.

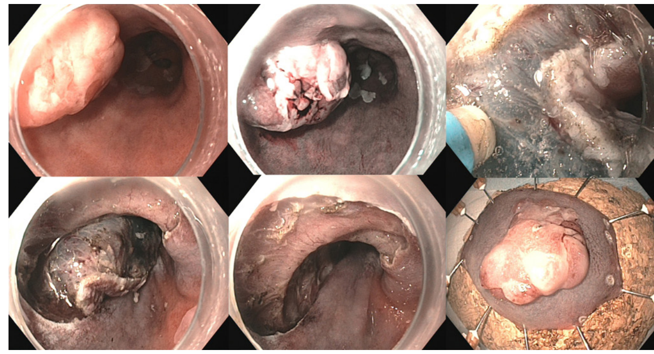

Figure 1 20 mm Paris Is lesion resected by endoscopic submucosal dissection. En bloc, R0-excision with clear peripheral and deep margins. Final histology revealing T1b adenocarcinoma with no adverse features. Considered a curative resection. Subsequently underwent endoscopic surveillance, with no local or regional recurrence at 35 months of follow-up.

General inclusion criteria included all patients undergoing EMR or ESD for Barrett's-associated dysplasia or adenocarcinoma, where the procedure targeted a distinct index (de novo) lesion. Resections performed for residual or locally recurrent disease at a prior resection site were excluded, while multiple de novo lesions in the same patient were included as separate cases. Participants under the age of 16 or those who could not consent were also excluded. Technique, equipment and post-resection management are detailed in online supplemental materials.

Variables prospectively collected included extent of Barrett's oesophagus by Prague classification, lesion location, size and procedure type (EMR or ESD). Pathology data included clearance of margins and presence of adverse risk factors including lymphovascular invasion, degree of differentiation and depth of invasion. Periprocedural adverse events, including delayed bleeding and deep mural injury, were recorded. Postprocedural outcomes included surgery, recurrence at surveillance and stricture formation.

Outcomes

The *primary outcome* was basal R0 excision. *Secondary outcomes* of interest included curative resection, rates of surgery, luminal recurrence detected at surveillance endoscopy, treatment of recurrences and adverse events.

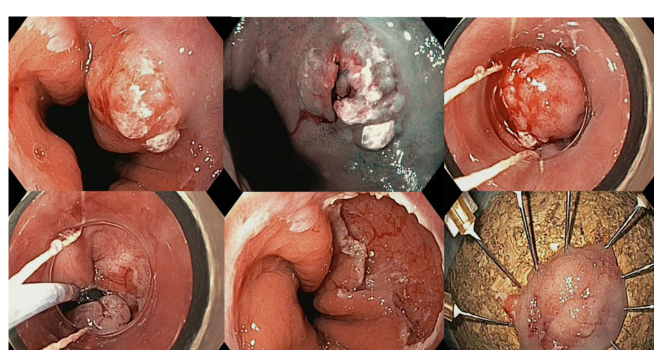

Figure 2 10 mm Paris IIa lesion resected by endoscopic mucosal resection. En bloc, R0-excision with clear peripheral and deep margins. Final histology revealed T1 adenocarcinoma with lymphovascular invasion. Subsequently underwent endoscopic surveillance due to frailty, with no local or regional recurrence at 61 months of follow-up.

To account for differences in follow-up duration between study periods, recurrence was defined as histological evidence of high-grade dysplasia (HGD) or adenocarcinoma at the site of the post-resection scar occurring within 2 years of the index endoscopic resection. This fixed follow-up window was chosen to standardise recurrence assessment across eras and minimise bias related to unequal surveillance duration.

Basal R0 excision was defined as the adenocarcinoma being clear of the deep margin. A curative resection was defined as a basal R0 excision, with histology showing well-to-moderate differentiation, ≤SM1 (≤500 µm) depth of invasion, and an absence of lymphovascular invasion. This encompasses both 'very low risk' and 'low risk' resections as per European Society of Gastrointestinal Endoscopy (ESGE) 2022 guidelines.[10]

Statistical analysis

SPSS V.26.0 (IBM Corp, New York, USA) was used for data analysis. Continuous variables were summarised as median and IQR. Categorical variables were recorded as frequencies (%). Pearson χ^2 or Fisher's exact tests were used to test for association between categorical variables, as appropriate. Independent t-tests were used for comparisons between continuous variables. Median follow-up time and IQR were determined using the reverse Kaplan-Meier method. Survival analyses were performed using the Kaplan-Meier method and log-rank statistics. A Cox proportional hazards model was used to assess risk factors for recurrence. All statistical significance levels were set at $p<0.05$ (two tailed).

RESULTS

Study population and follow-up

A total of 581 resections were performed in 542 patients. Median age was 70 years and 82.1% were male. Median lesion size was 20 mm (IQR 10–28). Median Prague classification was C2 (IQR 0–6) M4 (IQR 2–8). Overall, EMR was performed in 355 cases (61.1%) and ESD in 226 (38.9%) (table 1). Procedure duration was longer for ESD than EMR (101.5±54.9 vs 41.6±18.2 min, $p<0.001$).

Period 1 and 2 cohorts comprised 189 (32.5%) and 392 (67.5%) resections, respectively. Histological findings are displayed in online supplemental table S1. Briefly, in the entire cohort over the two periods, 52.4% of cases were either non-dysplastic (n=66) or dysplastic (79 low grade and 159 high grade). Of the 47.6% cancers (n=277), six were upstaged to T2 on final histology and were excluded from T1-specific analyses. Of the remaining 271 T1 cancers, 178 were stage T1a (65.7%) and 93 (34.3%) were stage T1b (53.7% SM1 and remaining SM2 or SM3). Following a diagnosis of T1 cancer, 31 of 271 patients (11.4%) proceeded to secondary surgical resection.

Following endoscopic resection of T1 cancer, median duration of surveillance was 30 months (IQR 14–57) after EMR and 20 months (IQR 10–35) after ESD. When stratified by histology, patients with T1a disease were followed for a median of 25 months (IQR 11–44), while those with T1b disease had a median follow-up of 19 months (IQR 10–36). After excluding the 31 patients who proceeded to surgery, recurrence surveillance data were available for 230 of 240 patients with T1 cancer (92%).

Comparison of the two study periods: resection outcomes

Overall, period 2 had a higher rate of T1 cancer (period 1 34.9% vs period 2 52.3%, $p<0.001$), greater representation of T1b disease (11.1% vs 18.4%, relative increase of 65.8%, p=0.025) and increased ESD utilisation (21.2% vs 77.1%, $p<0.001$) compared with period 1 (figure 3). In period 1 (n=189), 89.9% of resections were performed using EMR and only 10.1% using ESD. In contrast, the period 2 cohort showed a more balanced distribution, with 47.2% EMR and 52.8% ESD, reflecting changes in referral patterns and case selection. For all lesions treated by EMR, there was an increase in the proportion non-malignant lesions from period 1 to period 2 (69.4% vs 74.6%, p=0.015). Detailed resection outcomes are shown in table 2 and figure 4.

Table 1 Basic patient, lesion and procedure characteristics across both periods (all patients)

	Median (IQR), mean (SD) or %
Age	70 years (63–77)
Male gender	82.1
Comorbidities	
Diabetes	10.4
Cardiovascular disease	27.0
Renal disease	5.6
Pulmonary disease	8.3
Haematological disorder	1.0
Paris classification	
Is	12.8
IIa or IIb	57.8
IIa+Is OR Is	8.8
IIc component	20.6
Lesion size	20 mm (10–28)
Prague classification	C2 (0–6) M4 (2–8)
Type of endoscopic resection	
ESD	226 (38.9)
EMR	355 (61.1)
Procedure duration	
ESD	101.5±54.9 min
EMR	41.6±18.2 min
Deep mural injury	1.4
Delayed bleeding	0.9

EMR, endoscopic mucosal resection; ESD, endoscopic submucosal dissection.

In period 1, EMR was performed in 100% (23/23) of non-dysplastic and 95% (95/100) of dysplastic lesions, as well as in 84.4% of T1a cancers and 66.7% of T1b cancers. ESD was performed in only 19 cases during this period, primarily for lesions suspected of deeper invasion. Final histology of ESD cases revealed T1a and T1b cancer in seven cases each. Accordingly, the positive predictive value of endoscopy and ancillary tests for selecting ESD for deep cancer invasion only was 36.8% (7/19). Overall R0 and curative resection rates for this period were 69.7% and 56.1%, respectively.

In period 2, EMR was still performed for 95.3% (41/43) of non-dysplastic and 70.3% (97/138) of dysplastic lesions. However, ESD became the predominant technique for cancers (T1a 66.9% and T1b 95.8%). Overall R0 and curative resection rates for this period were 91.2% and 63.9%, respectively. These increases were more prominent for stage T1b but also present in stage T1a.

Comparing period 2 with period 1, R0 resection in stage T1a increased from 86.7% to 91.2% (p=0.021), and for T1b from 33.3% to 81.9% ($p<0.001$). Curative resection following current guidelines (including T1b-SM1 as low-risk) was similar between periods for all cancers (56.1% vs 63.9%, p=0.254) but

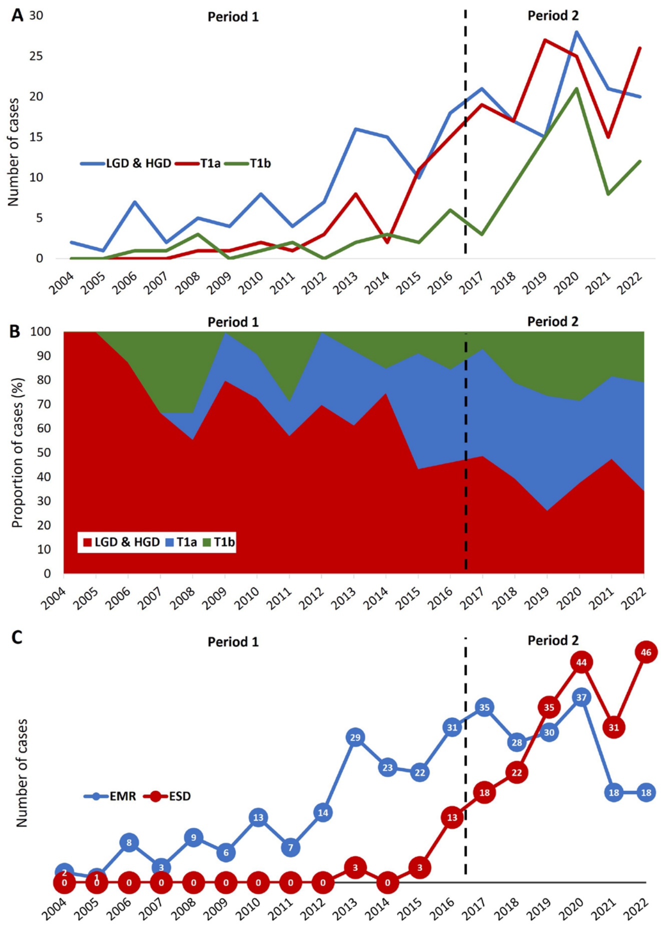

Figure 3 (A) Endoscopic resections performed for Barrett's dysplasia, T1a and T1b disease over time. (B) Proportion of cases over time by histology. (C) Endoscopic resection over time by technique. EMR, endoscopic mucosal resection; ESD, endoscopic submucosal dissection; HGD, high-grade dysplasia; LGD, low-grade dysplasia.

increased for stage T1b from period 1 to period 2 (from 9.5% to 30.5%, p=0.043).

Overall oncological outcomes

Overall, 31 of 271 patients proceeded to surgical resection (12 from period 1 and 19 from period 2). Surgical histology was available in 20 cases (7 from period 1 and 13 from period 2). Residual luminal disease was identified in 7/20 cases, comprising 1 T1a lesion, 4 T1b lesions and 2 cases of unspecified T1 disease. Lymph node metastases were identified in 2/20 cases, with a mean of 25 lymph nodes sampled per patient (range 13–41).

Across the full cohort, recurrence following EMR occurred at a median of 3 months (IQR 2–13), compared with a median of 8 months (IQR 4–13.5) following ESD. When stratified by histology, recurrence for T1a disease occurred at a median of 4 months (IQR 4–4), while for T1b disease it occurred at a median of 6.5 months (IQR 3.25–12.25). Given the variability in follow-up practice and duration, a Cox proportional hazards model was constructed (table 3). On multivariable analysis, independent predictors of recurrence were T1b histology (HR 9.07, 95% CI 2.14 to 38.36; p=0.003) and basal R1 resection (HR 5.87, 95% CI 1.69 to 19.84; p=0.005).

Among the 15 patients who developed luminal recurrence with cancer, 10 had undergone ESD and 5 EMR. Four occurred in period 1 (6.1% of all cancer) and 11 in period 2 (5.4% of all cancer, p=0.830). Recurrence was confined to the oesophagus in 10 patients, while 2 had concomitant lymph node metastases and 3 had synchronous distant metastases. At the time of index endoscopic resection, this subgroup was elderly and comorbid, with a median age of 77 years (IQR 72.1–77.9) and a median Charlson Comorbidity Index of 7 (IQR 5–7).

Management of malignant recurrence included repeat endoscopic resection in 6/15 patients (4 EMR and 2 ESD), further oncological therapy only in 4/15 (radiotherapy in 1, chemotherapy in 1, chemoradiotherapy in 1 and oesophagectomy in 1) and palliative management in 5/15 patients (palliative oesophageal stenting in 2 and symptom control alone in 3). During follow-up, 6/15 patients died at a median of 27 months (IQR 22–29), with death attributable to progressive disease in 5 cases. The remaining 9 patients remain alive out to a median follow-up of 49 months (IQR 16–85).

Among the 6/15 patients who underwent further endoscopic therapy, a single additional endoscopic resection was sufficient in 5 cases. These included three EMRs for T1a disease (one en bloc and two piecemeal) and two ESDs for T1a disease. One patient required two additional sessions of piecemeal EMR, both of which demonstrated T1b disease. This patient went on to have further radiotherapy.

Comparison of the two study periods: oncological outcomes

Results are shown in table 2 and figure 4. In period 1, with only 21.2% of cancers treated by ESD, the basal R0 rate was 69.7% and the curative resection rate was 56.1%. Consequently, recurrence of cancer or HGD occurred in 20.0%, and 2-year cancer-free survival was 90.8%. In period 2, 77.1% of cancers were treated by ESD. The basal R0 rate was significantly higher than in period 1 (91.2%, p<0.001), whereas the curative resection rate (63.9%, p=0.254) and recurrence of cancer/HGD (20.0%; p=0.075) did not differ significantly between periods. 2-year cancer-free survival in period 2 was similar at 92.5% (p=0.656).

Outcomes differed by tumour stage. For T1a cancers, the only significant difference between periods was basal R0 resection (96.2% vs 86.7%, p=0.021); other parameters were not significantly different. In contrast, for T1b cancers, period 2 showed significantly higher basal R0 rates (81.9% vs 33.3%, p<0.001), higher curative resection rates (30.5% vs 9.5%, p=0.043) and lower recurrence of cancer/HGD (23.6% vs 55.6%, p=0.048). 2-year cancer-free survival was numerically higher (62.2% vs 85.5%, p=0.255).

Comparison of resection techniques (both periods combined)

The comparative outcomes of ESD and EMR are summarised in table 1 and online supplemental figure S1. Among the 271 T1a/T1b cancers, ESD was the predominant resection modality (172/271, 63.5%). ESD was more commonly used for T1b disease than T1a disease (76/93, 81.7% vs 96/178, 53.9%; p<0.001).

In T1a cancers, lesions treated with ESD were significantly larger than those managed with EMR (31.1±18.6 mm vs 14.6±8.4 mm; p<0.001). Basal R0 resection trended higher with ESD compared with EMR (93/96, 96.9% vs 74/82, 90.2%; p=0.067). Curative resection rates were similar between modalities (ESD 77/96, 80.2% vs EMR 67/82, 81.7%; p=0.800). Rates of subsequent surgery after endoscopic resection were also comparable (ESD 3/96, 3.1% vs EMR 3/82, 3.7%; p=0.844). Luminal cancer/HGD recurrence did not differ between groups (ESD 4/90, 4.4% vs EMR 7/76, 9.2%; p=0.219). 2-year cancer-free survival was similar (98.6% EMR vs 98.9% ESD, p=0.650).

Table 2 Comparison of outcomes between period 1 and period 2, and between EMR and ESD

	Period 1 (n=189) (170 EMR, 19 ESD)	Period 2 (n=392) (185 EMR, 207 ESD)	P value (period 1 vs period 2)	EMR (n=355) period 1 n=170, period 2 n=185	ESD (n=226) period 1 n=19, period 2 n=207	P value (ESD vs EMR)
Dysplasia*						
Cases of EMR	95/100 (95.0)	97/138 (70.3)	**<0.001**	NA	NA	NA
T1a cancer	45/189 (23.8)	133/392 (33.9)	0.013	82/355 (23.1)	96/226 (42.5)	**<0.001**
Cases of ESD	7/45 (15.6)	89/133 (66.9)	**<0.001**	NA	NA	NA
R0 (basal) excision	39/45 (86.7)	128/133 (96.2)	**0.021**	74/82 (90.2)	93/96 (96.9)	**0.067**
Low-risk histology	40/45 (88.9)	114/133 (85.7)	0.590	74/82 (90.2)	80/96 (83.3)	0.178
Curative resection	35/45 (77.8)	109/133 (82.0)	0.538	67/82 (81.7)	77/96 (80.2)	0.800
Surgery	3/45 (6.7)	3/133 (2.3)	0.156	3/82 (3.7)	3/96 (3.1)	0.844
Recurrence of Ca†	1/41 (2.4)	2/125 (1.6)	0.726	1/76 (1.3)	2/90 (2.2)	0.662
Recurrence of Ca/HGD†	5/41 (12.2)	6/125 (4.8)	0.099	7/76 (9.2)	4/90 (4.4)	0.219
2-year cancer-free survival	97.2%	99.2%	0.717	98.6%	98.9%	0.650
T1b cancer	21/189 (11.1)	72/392 (18.4)	**0.025**	17/355 (4.8)	76/226 (33.6)	**<0.001**
Cases of ESD	7/21 (33.3)	69/72 (95.8)	**<0.001**	NA	NA	NA
R0 (basal) excision	7/21 (33.3)	59/72 (81.9)	**<0.001**	7/17 (41.2)	59/76 (77.6)	**0.003**
Low-risk histology	7/21 (33.3)	23/72 (31.9)	0.905	7/17 (41.2)	23/59 (30.3)	0.384
Curative resection	2/21 (9.5)	22/72 (30.5)	**0.043**	2/17 (11.8)	21/59 (28.9)	0.143
Surgery	9/21 (42.9)	16/72 (22.2)	**0.061**	5/17 (29.4)	20/59 (26.3)	0.795
Recurrence of Ca†	3/9 (33.3)	9/55 (16.4)	0.227	4/9 (44.4)	8/55 (14.5)	**0.033**
Recurrence of Ca/HGD†	5/9 (55.6)	13/55 (23.6)	**0.048**	6/9 (66.7)	12/55 (21.8)	**0.006**
2-year cancer-free survival	62.2%	85.5%	0.255	50%	87.4%	**0.021**
All cancers (T1a/T1b)	66/189 (34.9)	205/392 (52.3)	**<0.001**	99/355 (27.9)	172/226 (76.1)	**<0.001**
Cases of ESD	14/66 (21.2)	158/205 (77.1)	**<0.001**	NA	NA	NA
R0 (basal) excision	46/66 (69.7)	187/205 (91.2)	**<0.001**	81/99 (81.8)	152/172 (88.4)	0.135
Low-risk histology	47/66 (71.2)	137/205 (66.8)	0.507	81/99 (81.8)	103/172 (59.9)	**<0.001**
Curative resection	37/66 (56.1)	131/205 (63.9)	0.254	69/99 (69.7)	99/172 (57.6)	**0.047**
Surgery	12/66 (18.2)	19/205 (9.3)	**0.048**	8/99 (8.1)	23/172 (13.4)	0.188
Recurrence of Ca†	4/50 (8.0)	11/180 (6.1)	0.632	5/85 (5.9)	10/145 (6.9)	0.764
Recurrence of Ca/HGD†	10/50 (20.0)	19/180 (10.6)	0.075	13/85 (15.3)	16/145 (11.0)	0.348
2-year cancer-free survival	90.8%	92.5%	0.656	95.1%	91.3%	0.701

*66 non-dysplastic cases not included in this Table.
†10 of 240 cases without data on recurrence due to loss to follow-up.
Ca, cancer; EMR, endoscopic mucosal resection; ESD, endoscopic submucosal dissection; HGD, high-grade dysplasia; NA, not applicable.

In T1b cancers, lesions selected for ESD were likewise significantly larger than those treated with EMR (33.8±18.0 mm vs 18.1±13.8 mm; p=0.001). The rate of basal R0 resection was significantly higher following ESD than EMR (59/76, 77.6% vs 7/17, 41.2%; p=0.003). Curative resection rates remained numerically higher with ESD but did not reach statistical significance (ESD 21/76, 28.9% vs EMR 2/17, 11.8%; p=0.143). Rates of post-resection surgery were similar between groups (ESD 20/76, 26.3% vs EMR 5/17, 29.4%; p=0.795). Luminal recurrence of cancer/HGD was significantly lower after ESD compared with EMR (12/55, 21.8% vs 6/9, 66.7%; p=0.006). 2-year cancer-free survival was better following ESD (87.4% vs 50% EMR, p=0.021).

Adverse events

Among the 271 patients with T1a/T1b cancer, deep muscle injury requiring clip closure occurred in 6 cases (ESD 5/172, 2.9% vs EMR 1/99, 1.0%; p=0.421). Delayed bleeding was observed in 2 cases (ESD 2/172, 1.2% vs EMR 0/99, 0%; p=0.535). Post-resection strictures requiring at least one endoscopic dilation occurred in 95 cases (16.4%) and were significantly more common after ESD (n=51, 22.6%) compared with EMR (n=44, 12.4%; p=0.002). The total number of dilations performed did not differ between the ESD and EMR groups (p=0.544).

DISCUSSION

Our large retrospective study comparing two eras of lesion allocation demonstrates a clear temporal increase in procedural volume and oncological complexity in Barrett's neoplasia. The proportion of T1 cancers increased from 34.9% in period 1, when ESD was largely reserved for lesions suspected of deep invasion, to 52.3% in period 2, when ESD was applied to all cancers >15 mm. This shift was driven by a 65.8% increase in T1b cases, reflecting greater depth of invasion in the treated cohort. In response to this increasing oncological burden, treatment strategy evolved toward greater use of ESD for cancer, without displacement of EMR. Instead, for all cases treated by EMR, the proportion of non-malignant disease increased (69.4% to 74.6%), indicating preservation of technique. Despite treating more advanced disease, oncological outcomes improved, with basal R0 excision for all T1 cancers increasing from 69.7% to 91.2%. Importantly, the greatest improvements were observed in T1b disease, where basal R0 resection more than doubled, curative resection increased threefold and recurrence declined

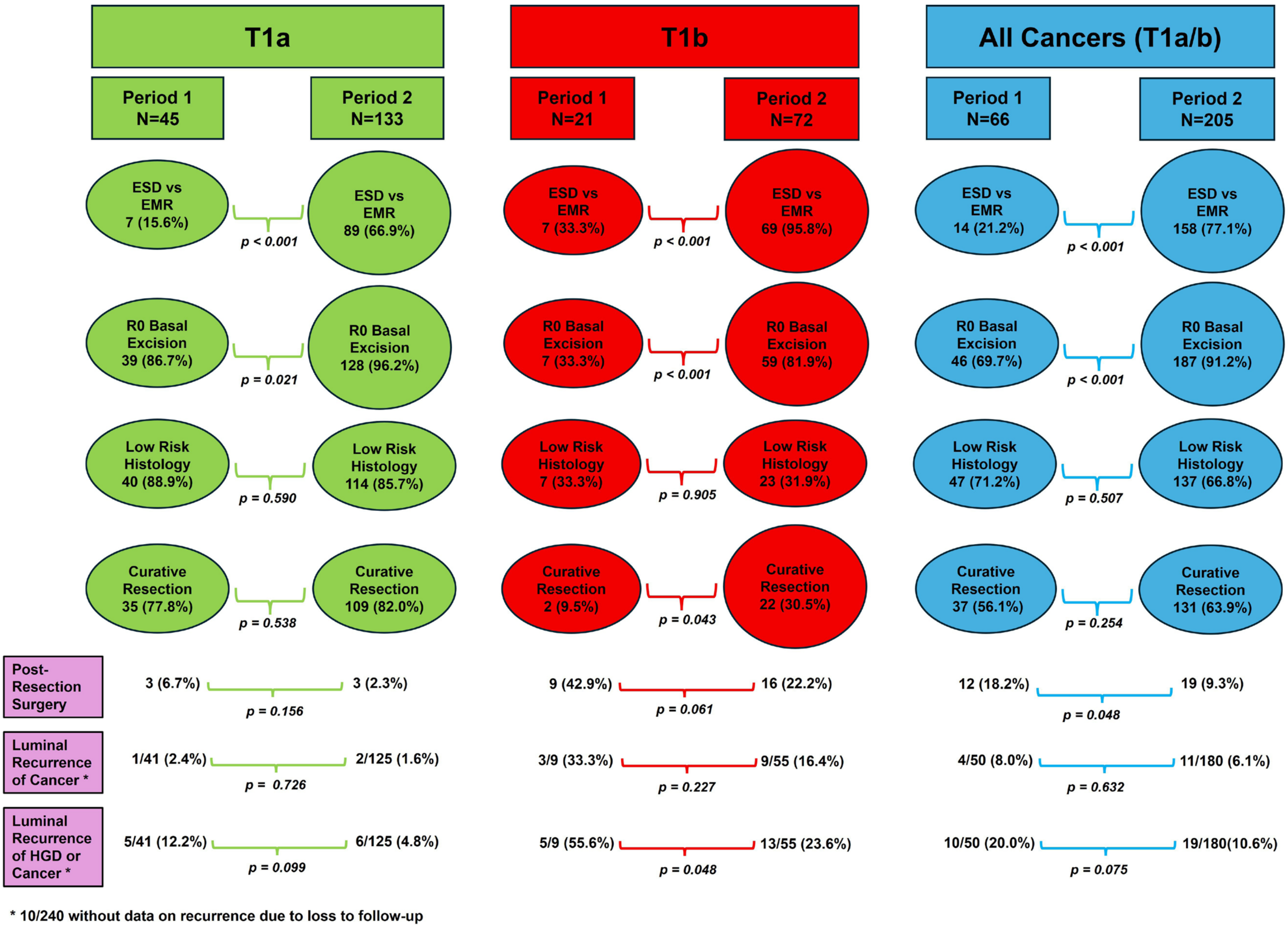

Figure 4 Outcomes of endoscopic resection for T1a and T1b disease stratified by time period. EMR, endoscopic mucosal resection; ESD, endoscopic submucosal dissection; HGD, high-grade dysplasia.

significantly. A favourable signal towards improved 2-year cancer-free survival was also observed for T1b disease (85.5% vs 62.2%). Collectively, these findings demonstrate improved local oncological outcomes with a selective strategy focused on achieving R0 excision of all cancers >15 mm with ESD.

For T1 oesophageal adenocarcinoma, endoscopic resection achieves disease-specific survival comparable to surgery, with fewer adverse events, shorter hospital stays, fewer readmissions and lower 90-day mortality.[23 24] However, optimal selection between EMR and ESD remains debated. Studies consistently demonstrate superior R0 resection with ESD, including the only randomised trial (59% vs 12%, p=0.01)[19] and a recent large retrospective cohort (58% vs 20%, p<0.01).[20] Other studies report higher curative resection rates (21% vs 11%, p<0.001)[21] and substantially lower recurrence with ESD (3.5% vs 31.4%, p<0.001).[22] In our cohort, outcomes for T1a disease were excellent with either modality. Basal R0 resection rates were high for both ESD and EMR (96.9% vs 90.2%), with no differences in curative resection (80.2% vs 81.7%) or recurrence (4.4% vs 9.2%). This confirms that mucosal disease can be adequately treated by either technique. In contrast, ESD was clearly superior for T1b lesions. Basal R0 resection was higher with ESD (77.6% vs 41.2%), and recurrence substantially lower (14.5% vs 44.4%), consistent with the biological requirement for a deeper submucosal excision. Accordingly, in period 2, this translated into near-universal use of ESD for T1b cancers (95.8%), while its use in T1a disease remained selective (66.9%), underscoring ESD as the preferred modality for submucosal invasion while preserving flexibility for mucosal lesions.

Current guidelines support selective use of ESD but rely heavily on subjective optical assessment. ESGE[10] recommends ESD for suspected T1b lesions and 'malignant lesions' >20 mm, with EMR reserved for lesions ≤20 mm and a low likelihood of submucosal invasion.[10] Similarly, American Society of Gastrointestinal Endoscopy (2023) advises ESD for suspected non-ulcerated T1 lesions that are 'bulky' or >20 mm, and either EMR or ESD for lesions ≤20 mm.[11] However, optical staging remains inaccurate, with expert sensitivity for identifying T1b disease of only 43.8%.[18] In contrast, our period 2 strategy applies two objective criteria. ESD is selected for lesions suspected to be at least T1a and >15 mm. This approach prioritises oncological adequacy over imperfect optical staging and is supported

Table 3 Cox-proportional hazard model for risk factors for recurrence

Characteristic	Univariate HR (95% CI)	P value	Multivariate HR (95% CI)	P value
EMR vs ESD	1.23 (0.42 to 3.61)	0.703	1.81 (0.40 to 8.18)	0.442
T1b vs T1a	11.92 (3.36 to 42.31)	**<0.001**	9.07 (2.14 to 38.36)	**0.003**
Period 1 vs period 2	1.30 (0.41 to 4.08)	0.658	1.82 (0.34 to 9.75)	0.483
Basal R1 vs R0	11.09 (4.00 to 30.75)	**<0.001**	5.87 (1.69 to 19.84)	**0.005**

EMR, endoscopic mucosal resection; ESD, endoscopic submucosal dissection.

by the high sensitivity for distinguishing T1 disease from HGD (89.1%),[18] as well as the high basal R0 resection rates achieved for both T1a (96.2%) and T1b lesions (81.9%).

Achieving a basal R0 excision is particularly critical in T1b disease. Historical surgical series reported lymph node metastasis rates of 27–44% for T1b cancers.[25–28] However, more contemporary endoscopic data suggest that this risk may be as low as 0–2% in carefully selected low-risk cases.[29 30] Thus, the quality of endoscopic resection has become a key determinant of oncological outcome. In our cohort, despite similar proportions of low-risk histology between periods (~30%), basal R0 resection for T1b disease improved markedly in period 2 (81.9% vs 33.3%, $p<0.001$). This was associated with higher curative resection rates (30.5% vs 9.5%, $p=0.043$) and fewer patients proceeding to surgery (22.2% vs 42.9%). Consistent with this, basal R1 excision independently increased recurrence risk more than fivefold (HR 5.87), underscoring the importance of achieving a basal R0 margin to avoid repeat endoscopic resection, additional oncological therapy or oesophagectomy.

These gains occurred alongside a clear shift towards resection of more advanced Barrett's neoplasia. The proportion of T1 cancers increased from 34.9% to 52.3%, driven by a rise in T1b disease from 11.1% to 18.4% (relative increase of 65.8%). In parallel, ESD utilisation increased from 21.2% to 77.1%. Despite increased tumour stage and procedural complexity, overall oncological outcomes remained stable, with 2-year cancer-free survival of 92% and no difference between periods ($p=0.656$). Importantly, disease control improved in T1b disease. Recurrence declined from 55.6% to 23.6% ($p=0.048$), curative resection increased from 9.5% to 30.5% ($p=0.043$) and 2-year cancer-free survival numerically increased from 62.2% to 85.5% ($p=0.255$). These improvements were underpinned by marked gains in basal R0 resection for T1b lesions (33.3% to 81.9%; $p<0.001$). Collectively, these findings demonstrate that the period 2 strategy enabled safe and effective management of an increasingly advanced Barrett's cancer case mix without compromising oncological outcomes.

Emerging evidence from an ongoing international trial suggests that lymph node metastasis following R0 endoscopic resection of high risk T1b lesions may be as low as 6% at a median follow-up of 22 months.[29] This is comparable to mortality associated with oesophagectomy in expert centres (~2%).[3] Together, these data support an expanding role for organ-preserving endoscopic therapy beyond frail or elderly patients. Consistent with this shift, progression to surgery in our cohort was less frequent in period 2 than in period 1 (22.2% vs 42.9%, $p=0.061$), likely reflecting both higher curative resection rates and increasing acceptance of endoscopic surveillance in selected high-risk patients. Furthermore, 2-year cancer-free survival was superior for T1b disease with ESD (87.4% vs 50%, $p=0.021$). Critically, this approach is contingent on achieving a basal R0 excision, making appropriate allocation between EMR and ESD fundamental. Thus, in this emerging era of organ-sparing endoscopic resection, our data underscore the importance of a selective approach that advocates ESD for any lesion suspected to be ≥T1a and >15 mm in size.

Importantly, implementation of the period 2 strategy did not result in overtreatment of non-malignant Barrett's lesions. EMR became increasingly concentrated in lower risk disease, with the proportion of non-malignant lesions treated with this modality increasing from 69.4% to 74.6%. In parallel, EMR use for invasive cancer declined sharply, for both T1b (66.7% to 4.2%) and T1a disease (84.4% to 33.1%), reflecting more appropriate triage of malignant lesions toward ESD. Despite 22.9% of T1 cancers being treated by EMR in period 2, overall oncological quality remained high, with a basal R0 resection rate of 91.2%. This confirms that ESD did not replace EMR, but rather expanded resection capability for higher risk disease while preserving efficiency and throughput for lower risk lesions. Reassuringly, this selective escalation in technique was not associated with compromised safety. Rates of deep muscle injury (2.9% vs 1.0%) and delayed bleeding (1.2% vs 0%) did not differ significantly between ESD and EMR. Collectively, these findings demonstrate that a selective strategy enables safe, efficient and sustainable allocation between EMR and ESD without over-burdening the endoscopy unit.

This study has limitations. It was conducted in two expert Barrett's centres; however, endoscopic resection of suspected Barrett's adenocarcinoma should be restricted to such settings. The long study period introduces potential confounding from technological advances, increasing operator experience and evolving referral patterns. Follow-up duration also differed between periods, although recurrence was assessed using Cox regression to account for this. Finally, both band and cap EMR techniques were included. Results were presented together, as separating this data would result in an underpowered analysis. However, prior studies have demonstrated that both techniques yield similar results.[12]

In summary, adopting a selective resection algorithm that prioritises ESD for all suspected ≥T1a lesions >15 mm significantly improved R0 excision, curative resection rates and recurrence outcomes, particularly for T1b disease, without increasing overtreatment of low-risk Barrett's neoplasia. Combined with the observed short-term survival advantage for T1b disease managed with ESD, these findings support routine use of ESD for all larger Barrett's cancers. This approach facilitates safe, organ-preserving management of an increasingly advanced Barrett's cancer case mix and is readily implementable in expert centres to optimise oncological outcomes.

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