Thieme

Adherence to guideline recommendations for Barrett's esophagus (BE) surveillance endoscopies: Effects of dedicated BE endoscopy lists

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ABSTRACT

Background and study aims For non-dysplastic Barrett's Esophagus (BE) patients, guidelines recommend endoscopic surveillance every 3 to 5 years with four-quadrant random biopsies every 2 cm of BE length. Adherence to these guidelines is low in clinical practice. Pooling BE sur-

veillance endoscopies on dedicated endoscopy lists performed by dedicated endoscopists could possibly enhance guideline adherence, detection of visible lesions, and dysplasia detection rates (DDRs).

Patients and methods Data were used from the ACID-study (Netherlands Trial Registry NL8214), a prospective trial of BE surveillance in the Netherlands. BE patients with known or previously treated dysplasia were excluded. Guideline adherence, detection of visible lesions, and DDRs were compared for patients on dedicated and general endoscopy lists.

Results A total of 1,244 patients were included, 318 on dedicated lists and 926 on general lists. Endoscopies on dedicated lists showed significantly higher adherence to the random biopsy protocol (85% vs. 66%, P <0.01) and recommended surveillance intervals (60% vs. 47%, P <0.01) compared to general lists. Detection of visible lesions (8.8% vs. 8.1%, P = 0.79) and DDRs were not significantly different (6.9% and 6.6%, P = 0.94). None (0.0%) of the patients scheduled on dedicated lists and 10 (1.1%) on general lists were diagnosed with esophageal adenocarcinoma (P = 0.07). In multivariable analysis, dedicated lists were significantly associated with biopsy protocol adherence and adherence to surveillance interval recommendations with odds ratios of 4.45 (95% confidence interval [CI] 2.07–9.57) and 1.64 (95% CI 1.03–2.61), respectively.

Conclusions Dedicated endoscopy lists are associated with better adherence to the random biopsy protocol and surveillance interval recommendations.

Introduction

Over the past decades, the incidence of esophageal adenocarcinoma (EAC) has increased in Western populations [1, 2]. Prognosis of patients with EAC depends largely on the stage of diagnosis. The overall 5-year survival rate is poor at approximately 20% [3]. Yet, mortality rates are exceedingly low in EAC for which endoscopic therapy is considered feasible [4, 5].

Barrett's esophagus (BE) is an established risk factor for EAC. To detect EAC in an early and treatable stage, periodic surveillance endoscopies are advised for BE patients [6, 7, 8, 9, 10]. In the Netherlands, the majority of BE surveillance endoscopies are performed in community hospitals. These patients are solely non-dysplastic BE (NDBE) patients, since BE patients with known or suspected dysplasia and EAC are referred to tertiary referral centers for treatment and follow-up.

According to current international guidelines, adequate NDBE surveillance endoscopies encompass minute inspection of the BE segment with targeted biopsies in the presence of visible lesions [6, 7, 8, 9, 10]. In addition, random four-quadrant biopsies should be obtained every 2 cm of BE length [6, 7, 8, 9, 10]. In the absence of dysplasia, surveillance endoscopies should be repeated at 5- and 3-year intervals, for BE segments of 1 to 3 cm and 3 to 10 cm, respectively [6, 10]. Patients with extremely long-segment NDBE (i. e. ≥10 cm) should be referred to a tertiary referral center for follow-up [8, 10].

It is well recognized that, in daily practice, adherence to the guideline recommendations of four-quadrant random biopsies and surveillance intervals recommendations is low. Although previous studies have shown increased dysplasia detection rates in case of adherence to the random biopsy protocol [8, 11, 12], a recent meta-analysis reported that an adequate number of biopsies is obtained in only half of BE surveillance endoscopies [13]. Similarly, adherence to recommendations on the BE surveillance intervals was estimated to be only 55% in the same meta-analysis [13].

The organization of BE surveillance care may differ per community hospital. In most hospitals in the Netherlands, incidental BE surveillance endoscopies are performed on general endoscopy lists, mixed with endoscopies for other indications, and performed by all endoscopists. Yet in some hospitals, BE surveillance endoscopies are clustered on a dedicated endoscopy list. These dedicated BE endoscopy lists are performed by few experienced endoscopists with special interest in BE.

This clustering of BE surveillance endoscopies on dedicated endoscopy lists could potentially improve BE surveillance care by increased guideline awareness and adherence. In addition, it could lead to enhanced recognition of dysplastic lesions, because few endoscopists gain considerable experience in performing BE surveillance endoscopies. The aim of our study, therefore, was to evaluate both adherence to the random biopsy protocol and to the recommended surveillance intervals in BE surveillance endoscopies performed in community hospitals, and to compare these measures between surveillance endoscopies performed on dedicated BE lists and those scheduled on general endoscopy lists. We also wished to compare detection rates of visible lesions and dysplasia between these two groups.

Patients and methods

For the current study, we used data from the ACID-study database (Netherlands Trial Registry NL8214), an ongoing prospective study on BE surveillance. The ACID-study is a stepped wedge cluster randomized study that evaluates the added value of acetic acid chromoendoscopy for the detection of dysplasia and EAC in BE patients. In total 18, Dutch community hospitals participate in this study, with data entry since October 2019. The study was approved by the medical ethics review boards of all participating hospitals. All patients provided written consent for data collection.

General endoscopy lists and dedicated BE lists

In 15 of the 18 participating community hospitals, BE surveillance was organized such that surveillance endoscopies were scheduled on general endoscopy lists performed by general

endoscopists, including residents in training. General lists included incidental BE surveillance procedures mixed with endoscopies for other indications. The performing endoscopist was not necessarily the same endoscopist deciding on future surveillance intervals based on the histopathological results. The time allocation for each surveillance procedure varied among hospitals and ranged between 15 and 30 minutes.

In the other three community hospitals, BE surveillance was performed on dedicated BE lists. Dedicated BE lists were defined as endoscopy lists in which multiple BE surveillance endoscopies are clustered and consistently performed by the same endoscopists (i. e. one or two endoscopists per hospital). These dedicated endoscopists also decided on subsequent surveillance intervals based on histopathological findings. Similar to general endoscopy lists, time allocated to each surveillance endoscopy varied between 15 and 30 minutes. There was no standardized protocol for use of sedation. None of the dedicated BE endoscopists received additional training or guidance with respect to BE surveillance compared to general endoscopists. More importantly, none of the dedicated BE endoscopists were expert endoscopists in the treatment of neoplastic BE.

Dedicated BE endoscopy lists were not initiated for the purpose of the current study and no changes were made in routine clinical care.

Study population

We included patients with a biopsy-proven diagnosis of BE (i. e. Prague C&M classification [14] ≥C0M1 with intestinal metaplasia on histological examination) who were scheduled for regular BE surveillance. There was no upper limit for BE length to be considered eligible. We excluded: 1) patients previously treated for dysplasia or EAC; 2) patients with an intensified follow-up regimen due to previous dysplasia; 3) patients newly diagnosed with BE; and 4) patients in whom other factors precluded an adequate surveillance endoscopy, i. e. esophageal varices or reflux esophagitis grade C or D precluding endoscopic biopsies, or massive food retention during endoscopy.

Patients were categorized into two groups, depending on the way BE surveillance was organized in the respective hospitals. If BE surveillance endoscopies were scheduled on mixed, general endoscopy lists conducted by general endoscopists, patients were classified as “general endoscopy list patients”; if the BE care was organized with BE surveillance endoscopies clustered on dedicated endoscopy lists performed by dedicated endoscopists, patients were classified as “dedicated endoscopy list patients”.

Histopathological assessment

Biopsies obtained during surveillance endoscopies were routinely assessed by community hospital pathologists in all participating centers. Expertise and training of pathologists regarding BE neoplasia was similar for hospitals with general and dedicated lists. To ensure correct diagnosis of dysplasia, all biopsies with suspected dysplasia of any grade, or reported as “indefinite for dysplasia,” were centrally reviewed by at least one additional pathologist with expertise in gastrointestinal pathology.

Outcomes and definitions

Primary outcomes were adherence to the random four-quadrant biopsy protocol and to the recommended surveillance intervals.

Random four-quadrant biopsy protocol adherence was defined as a minimum of four random biopsies every 2 cm of circumferential BE extent, plus at least one biopsy every 2 cm of BE tongues. The actual number of random biopsies taken during the endoscopy was compared to the minimum number of biopsies that should be obtained according to our definition. A ratio <1 was defined as non-adherent; a ratio ≥1 as adherent. In the presence of visible lesions, targeted biopsies and random biopsies were summed.

We considered surveillance intervals as adequate if surveillance endoscopies were performed within 4.5 to 5.5 years for BE segments < 3 cm, and within 2.5 to 3.5 years for long-segment BE (≥ 3 cm), as in accordance with current guidelines [6, 10]. Non-adherence to surveillance intervals was defined as any interval outside this range. Patients with BE segments ≥10cm who received follow-up endoscopies were classified as adherent if the endoscopy was performed between 1.5 and 3.5 years. We chose this wider range as no specific guideline recommendations are available for these patients. Patients with a previous diagnosis of “indefinite for dysplasia” were excluded from the analyses concerning surveillance intervals.

Secondary outcomes were detection rates of visible lesions and dysplasia. The presence of visible lesions was defined as the presence of one or more visible lesions per patient. Dysplasia was defined as the presence of low-grade dysplasia (LGD), high-grade dysplasia (HGD) or EAC diagnosed on targeted or random biopsies, reviewed by expert gastrointestinal pathologists.

Data collection

Study data were collected and managed using REDCap electronic data capture tools hosted at St. Antonius Hospital [15, 16].

Data were registered prospectively from October 2019 to July 2022. Information about each patient was entered in the database only once. Data on follow-up endoscopies were not registered.

All data collection was done by one research fellow in a standardized format. Variables with missing data or outliers were manually checked to ensure data are accurate.

Statistical analysis

Means and standard deviations were used to describe normally distributed baseline characteristics. Medians with 25th and 75th percentiles (p25-p75) were reported for variables with a skewed distribution.

Differences in outcome variables between study groups were compared by Chi-square tests, Fisher’s exact tests, Wilcoxon rank sum tests or Mood’s Median tests where appropriate. In addition, guideline adherence and dysplasia detection rates were compared by using a hierarchical mixed-effects logistic regression model with a random intercept per hospital, to correctly account for both multilevel data and for possible

confounders. In any case, we included the use of acetic acid chromoendoscopy as a covariate for the multivariable analyses evaluating dysplasia detection and adherence to the random biopsy protocol, since this could be a possible confounder introduced by study design.

Because data were collected prospectively and in a standardized format, the percentage of missing data was expected to be a small proportion of the dataset. Missing values were omitted from the analyses if the missing rate was 5% or less.

Results

Patients

Of the 1,413 patients included in the ACID-study between October 2019 and July 2022, 1,244 patients met our inclusion criteria (▶ **Fig. 1**). A total of 318 included patients (26%) were scheduled on dedicated BE lists; 926 patients (74%) were scheduled on general endoscopy lists.

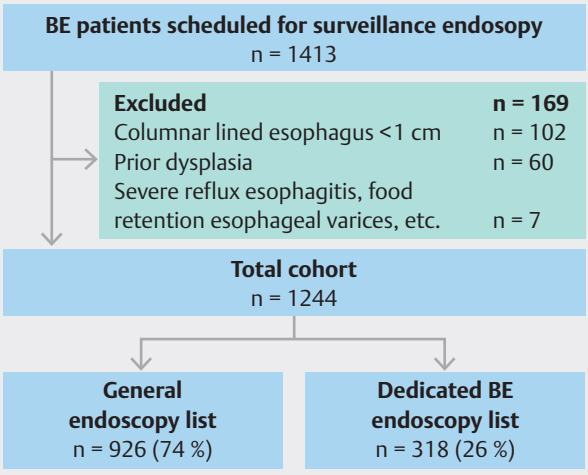
Characteristics of the included patients and their endoscopies are shown in ▶ **Table 1**. Mean age, gender, and median BE length were comparable. Endoscopies on dedicated lists had a shorter total procedure time compared to endoscopies on general lists, with a median of 6 minutes (p25–p75 5–9) versus 7 minutes (p25–p75 5–10), respectively (P <0.01). Acetic acid chromoendoscopy was used in 33% of endoscopies on dedicated endoscopy lists versus 7% on general lists (P <0.01). While sedation was more often administered on dedicated lists (74% versus 57% on general lists, P <0.01), high-definition endoscopes were more frequently used on general lists (99% versus 96% on dedicated lists, P <0.01).

Guideline adherence

Adherence to the random four-quadrant biopsy protocol was significantly better in endoscopies scheduled on dedicated BE lists, 85% versus 66% on general endoscopy lists (P <0.01) (▶ **Table 2**). In both groups, adherence to the random biopsy protocol decreased significantly (P <0.01 for trend) with increasing BE length (▶ **Fig. 2**).

▶ **Fig. 3** shows the number of years since the previous endoscopy for both general lists and dedicated BE lists patients, stratified by BE length. For patients with BE segments <3 cm, the median time since the previous endoscopy was 4.8 years (p25–p75 3.3–5.0 years) and 4.3 years (p25–p75 3.2–5.2 years) for dedicated BE lists and general lists, respectively (P = 0.049). For patients with BE length ≥3 cm, median time since the previous endoscopy was similar for dedicated lists (3.2 years [p25–p75 2.9–3.4]) and general lists (3.2 years [p25–p75 3.0–3.7]) (P = 0.39).

Adherence to surveillance intervals according to our predefined definition was higher in endoscopies on dedicated lists (60% vs. 47%, P <0.01). Higher adherence rates were seen in endoscopies on dedicated lists compared to general lists for both BE segments <3 cm (52% vs. 31%, P <0.01) and BE segments ≥3 cm (64% vs. 54%, P = 0.01) (▶ **Table 2**). In BE segments <3 cm, non-adherence to surveillance interval recommendations mainly resulted from surveillance intervals that were too short, in both dedicated and general lists (▶ **Fig. 4**). In BE segments ≥3 cm, surveillance intervals that were too long were the main reason of non-adherence in both groups. The median deviations from our predefined upper limit and lower limit of adequate surveillance intervals are presented in **Supplementary Table 1**.



▶ **Fig. 1** Patient inclusion.

Visible lesions and dysplasia detection

The prevalence of visible lesions detected during endoscopy was similar in both groups, with visible lesions detected in 28 patients (8.8%) and 75 patients (8.1%) on dedicated and general lists, respectively (P = 0.79) (▶ **Table 3**). The visible lesions were found to be dysplastic in two of 28 patients on dedicated lists (7.1%) and 20 of 75 patients (27%) on general endoscopy lists (P = 0.06).

Overall, dysplasia detection rates were comparable between groups (6.9% vs. 6.6%, P = 0.94) (▶ **Table 3**). On dedicated lists, most dysplastic cases were LGD. There were no diagnoses of EAC (0.0%) among dedicated list patients, whereas a total of 10 EACs (1.1%) were found during endoscopies on general lists (P = 0.07). Characteristics of the previous surveillance endoscopy of all EAC and HGD cases are listed in ▶ **Table 4**. Median BE length of patients with EAC and HGD was C3M5 (p25–p75 C2–6 and M3–7). For these patients, median time since previous endoscopy for BE segments <3 cm was 5.2 years (p25–p75 2.7–5.2) and for BE segments ≥3 cm 3.3 years (p25–p75 3.0–3.9). Two patients had their last surveillance endoscopy >15 years prior to their diagnosis of EAC. In 13 patients (54%) with a diagnosis of HGD or EAC, an insufficient number of biopsies was obtained during the previous endoscopy. All three patients (100%) diagnosed with HGD on dedicated lists could be treated by endoscopic resection with or without ablative therapy of the remaining BE segment, whereas this was the case for 16 of 23 patients (70%) diagnosed with HGD or EAC on general lists.

Of all 83 patients with dysplastic changes, 21 patients (25%) were diagnosed with targeted biopsies rather than random biopsies. Patients with dysplasia on general endoscopy lists

▶ **Table 1** Patient characteristics and endoscopic data.

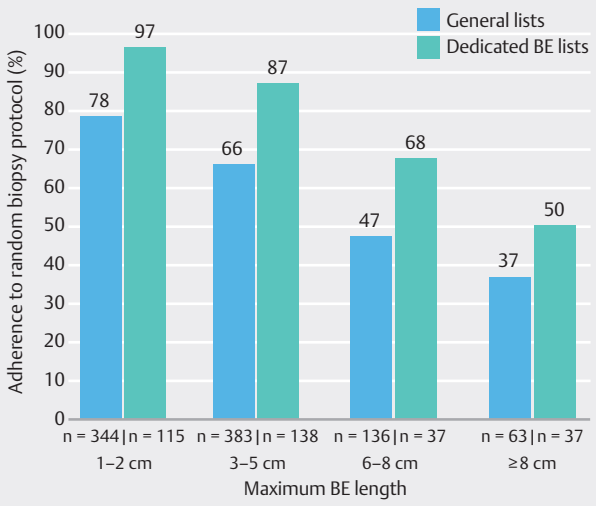
	Total cohort n = 1244	Dedicated BE lists n = 318	General lists n = 926	P value (dedicated vs. general)
Demographics				
Age, years, mean (SD)	65 (10)	65 (11)	65 (10)	0.34
Female sex, n (%)	385 (30.9)	90 (28.3)	295 (31.9)	0.27
ASA-score, n (%)				0.06
▪ **1**	192 (15.4)	45 (14.2)	147 (15.9)	
▪ **2**	912 (73.3)	250 (78.6)	662 (71.5)	
▪ **3**	80 (6.4)	12 (3.8)	68 (7.3)	
▪ **4**	1 (0.1)	0 (0.0)	1 (0.1)	
	59 (4.7%) missing	*11 (3.5%) missing*	*48 (5.2%) missing*	
Time since BE diagnosis, years, median (p25–p75)	8 (4–12)	8 (4–12)	8 (4–12)	0.96
	8 (0.6%) missing	*1 (0.3%) missing*	*7 (0.8%) missing*	
Surveillance endoscopies				
BE length, cm, median (p25–p75)				
▪ Prague C	1 (0–4)	1 (0–3)	1 (0–4)	0.09
▪ Prague M	3 (2–5)	3 (2–5)	3 (2–5)	0.33
Esophagitis, n (%)				0.80
Total	96 (7.7)	23 (7.2)	73 (7.9)	
▪ A	41 (3.3)	9 (2.8)	32 (3.5)	
▪ B	42 (3.4)	13 (4.1)	29 (3.1)	
▪ C	4 (0.3)	1 (0.3)	3 (0.3)	
▪ Grade not reported	9 (0.7)	0 (0.0)	9 (1.0)	
Sedation, n (%)				<0.01
Midazolam/fentanyl	761 (61.2)	234 (73.6)	527 (56.9)	
Propofol	85 (6.8)	26 (8.2)	59 (6.4)	
No sedation	398 (32.0)	58 (18.2)	340 (36.7)	
HD endoscopy, n (%)	1218 (97.9)	305 (95.9)	913 (98.6)	<0.01
	13 (1.0%) missing	*3 (0.9%) missing*	*10 (1.1%) missing*	
Acetic acid chromoendoscopy, n (%)	169 (13.6)	104 (32.7)	65 (7.0)	<0.01
Duration endoscopy, min, median (p25–p75)	7 (5–10)	6 (5–9)	7 (5–10)	<0.01
	41 (3.3%) missing	*3 (0.9%) missing*	*38 (4.1%) missing*	

ASA, American Society of Anesthesiologists; BE, Barrett's esophagus; HD, high-definition; SD, standard deviation.

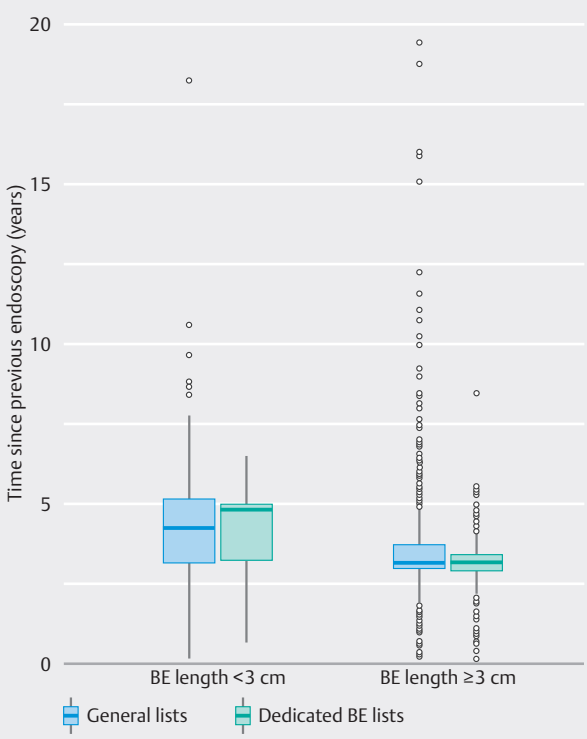
were more often diagnosed using targeted biopsies compared to patients with dysplasia on dedicated lists (20/61 patients [33%] vs. one of 22 patients [5%], P <0.01). Nine of 10 EAC patients (90%) on general endoscopy lists presented with visible lesions. There were no significant differences in the detection of LGD or HGD with targeted biopsies between the two groups (▶ **Table 3**).

Logistic regression analyses

In both univariable and multivariable analysis, dedicated BE endoscopy lists were significantly associated with random biopsy protocol adherence, with odds ratios (ORs) of 3.43 (95% confidence interval [CI] 1.77–7.21) and 4.45 (95% CI 2.07–9.57), respectively (▶ **Table 5**). Dedicated BE endoscopy lists were also significantly associated with adherence to re-



▶ **Fig. 2** Adherence to random 4Q biopsy protocol stratified by maximum BE length. Adherence was defined as four quadrant random biopsies every 2 cm of circumferential BE extent, plus at least one biopsy every 2 cm of BE tongues. In the presence of visible lesions, target biopsies and random biopsies were totalled.



▶ **Fig. 3** Boxplots showing the time since previous endoscopy in years for general endoscopy lists and for dedicated BE endoscopy lists, stratified by BE length. Within each box, the median time since previous endoscopy is indicated by the horizontal black line. The box encompasses the 25th and 75th percentiles of each group, whereas the vertical lines represent the values within 1.5 of the interquartile range of the 25th and the 75th percentiles. The dots denote outliers that fall above the upper fence or below the lower fence.

commended surveillance intervals (OR 1.75, 95% CI 1.12–2.78 for univariable analysis and OR 1.64, 95% CI 1.03–2.61 for multivariable analysis). ORs for total dysplasia detection in relation to dedicated BE lists were 1.05 (95% CI 0.61–1.82) and 0.96 (95% CI 0.53–1.70) and did not reach statistical significance. Finally, the lower odds of HGD/EAC detection on dedicated BE endoscopy lists were not statistically significant in univariable and multivariable analysis.

Discussion

In this prospective, multicenter study, we compared NDBE surveillance endoscopies scheduled on dedicated and general endoscopy lists in a community setting, rather than tertiary referral centers. We found that adherence to the random four-quadrant biopsy protocol and to the recommended surveillance intervals is significantly better in endoscopies on dedicated BE lists compared to those on general lists. The prevalence of visible lesions and total dysplasia detection rates did not differ between the two groups. Of all detected dysplasia, detection by targeted biopsies was higher on general endoscopy lists. Finally, although not significant, our study suggests that HGD and EAC are more often diagnosed in patients scheduled on general endoscopy lists.

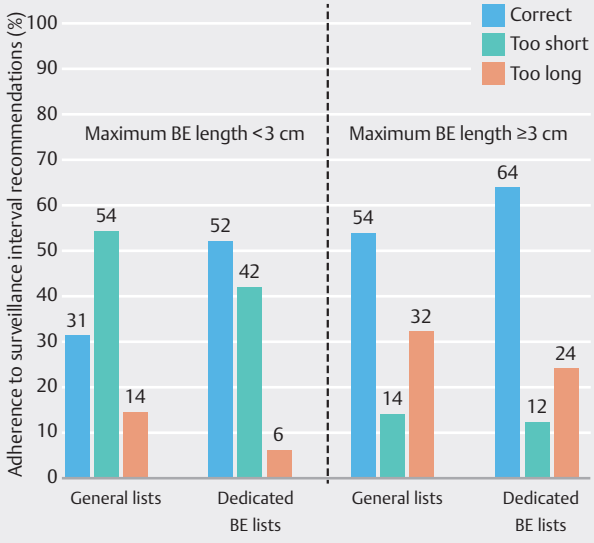
Previous studies evaluating the introduction of dedicated BE endoscopy lists also demonstrated higher rates of random biopsy protocol adherence in dedicated BE endoscopies [17, 18]. Ooi et al. compared biopsy protocol adherence of endoscopies on dedicated lists with a historical cohort of general lists [17]. The authors showed increased adherence from 10% to 77%. Britton et al. also demonstrated increased biopsy protocol adherence on dedicated lists, 72% versus 42% on general lists [18]. While these results indicate an improvement in BE surveillance care, both studies were prospective intervention studies rather than observational cohort studies, thereby potentially enlarging clinical effects. Moreover, the studies lacked correction for confounding factors in the analyses. Our study, therefore, is a better representation of clinical practice by reflecting the long-term improvement in BE surveillance care on dedicated endoscopy lists. We also present effect estimates based on multivariable regression analyses in order to correct for possible confounding.

Our study did not reveal a higher prevalence of visible lesions, nor a higher dysplasia detection rate on dedicated lists compared to general lists. Similar to our study, Britton et al. did not find a significant difference in dysplasia detection between dedicated and general lists [18]. Ooi et al. demonstrated a dysplasia detection rate of 18% on dedicated BE lists, compared to 8% in the historical cohort of endoscopies on general lists [17]. Importantly, one of the participating hospitals in the study of Ooi et al. was a tertiary referral center for dysplastic BE patients, which may have introduced some degree of selection bias. Moreover, in that study, procedure time was pro-

▶ **Table 2** Adherence to the random biopsy protocol and surveillance interval recommendations.

Outcomes	Total cohort n = 1244	Dedicated BE lists n = 318	General lists n = 926	*P* value (dedicated vs. general)
Biopsies per 2 cm maximum BE length, mean (SD)	3.8 (1.8)	4.3 (1.8)	3.6 (1.7)	<0.01
Adherence to random biopsy protocol*, n (%)	878 (70.6)	270 (84.9)	608 (65.7)	<0.01
Adherence to surveillance intervals†‡, n (%)				
BE length <3 cm				
▪ Adherence	138 (36.8)	51 (52.0)	87 (31.4)	<0.01
▪ Too short	191 (50.9)	41 (41.8)	150 (54.2)	0.048
▪ Too long	46 (12.3)	6 (6.1)	40 (14.4)	0.048
BE length ≥3 cm				
▪ Adherence	459 (56.4)	136 (63.8)	323 (53.8)	0.01
▪ Too short	111 (13.7)	26 (12.2)	85 (14.2)	0.55
▪ Too long	243 (29.9)	51 (23.9)	192 (32.0)	0.03

*Adherence was defined as four-quadrant random biopsies every 2 cm of circumferential BE extent, plus at least one biopsy every 2 cm of BE tongues. In the presence of visible lesions, target biopsies and random biopsies were summed.
†Adherence was defined as 3 years + /- 6 months, 5 years + /-6 months for BE length <3 cm and ≥3 to 10 cm respectively, and between 1.5 and 3.5 years for BE ≥10 cm.
‡40 cases with missing values and 16 cases with 'indefinite for dysplasia' as previous histology result were excluded from this analysis.
BE, Barrett's esophagus; SD, standard deviation.



▶ **Fig. 4** Adherence to surveillance interval recommendations for general and dedicated BE endoscopy lists. Surveillance intervals were considered adequate if surveillance endoscopies were performed within 4.5 to 5.5 years for BE segments <3 cm, within 2.5 to 3.5 years for BE segments ≥3 cm to 10 cm, and within 1.5 to 3.5 years for BE segments ≥10 cm.

longed in dedicated lists, and endoscopists received training in lesion detection from a BE expert endoscopist.

Although we did not demonstrate a higher overall dysplasia detection rate, we did find a trend toward higher HGD- and EAC detection rates on general endoscopy lists, which appears counterintuitive. Because our study has a non-randomized design, this could be attributed to selection bias. However, all included patients with known or previously treated dysplasia were excluded from analysis. We also excluded the initial (diagnostic) BE endoscopies, as these endoscopies are believed to contain a higher prevalence of dysplasia and EAC [19, 20] and are mostly scheduled on general endoscopy lists. In an attempt to explain the higher HGD and EAC detection rates on general endoscopy lists, we evaluated the histology results, surveillance interval, and number of random biopsies obtained on the previous surveillance endoscopy. In the majority of cases, an insufficient number of biopsies was obtained or the time interval since the previous endoscopy was too long according to the surveillance interval recommendations. The former finding suggests sampling error on the previous endoscopy. The enhanced adherence to the random biopsy protocol in combination with the higher rates of adherence to the surveillance interval recommendations on dedicated endoscopy lists could account for the frequent diagnoses of LGD rather than HGD and EAC. In this way, dedicated endoscopy lists could prevent the progression to HGD and EAC by early LGD diagnosis and subsequent referral for treatment and follow-up.

Surprisingly, we found that BE patients with dysplasia were more often diagnosed with targeted biopsy on general lists

▶ **Table 3** Detection of visible lesions and dysplasia detection rates in BE patients scheduled on dedicated and general lists.

Outcomes	Total cohort n = 1244	Dedicated BE lists n = 318	General lists n = 926	*P* value (dedicated vs. general)
Visible lesions, n (%)	103 (8.3)	28 (8.8)	75 (8.1)	0.79
Dysplastic visible lesions, n (%)	20/103 (19.4)	2/28 (7.1)	20/75 (26.7)	0.06
Dysplasia*, n (%)				
Total	83 (6.7)	22 (6.9)	61 (6.6)	0.94
▪ LGD	57 (4.6)	19 (6.0)	38 (4.1)	0.22
▪ HGD	16 (1.3)	3 (0.9)	13 (1.4)	0.77
▪ EAC	10 (0.8)	0 (0.0)	10 (1.1)	0.07
Dysplasia detection on targeted biopsy*, n (%)				
Total	21/83 (25.3)	1/22 (4.5)	20/61 (32.8)	0.01
▪ LGD	2/57 (3.5)	0/19 (0.0)	2/38 (5.3)	0.55
▪ HGD	10/16 (62.5)	1/3 (33.3)	9/13 (69.2)	0.52
▪ EAC	9/10 (90.0)	NA	9/10 (90.0)	NA

*Highest grade of dysplasia per patient.
BE, Barrett's esophagus; EAC, esophageal adenocarcinoma; HGD, high-grade dysplasia; LGD, low-grade dysplasia; NA, not applicable.

compared to dedicated lists, while one could hypothesize that this would be vice versa. One explanation could be that endoscopists on general lists inspect the BE segment more thoroughly. However, there was a higher prevalence of advanced dysplastic cases (i. e. HGD and EAC) in general lists compared to dedicated lists. Nine of 10 EAC cases on general lists presented as obvious visible lesions and were subsequently detected on targeted biopsy. We know from previous studies that HGD and EAC frequently present as visible lesions, while LGD is often invisible [5, 21]. Therefore, the higher proportion of targeted dysplasia detection on general lists could also be explained by the difference in degree of dysplasia.

Although better in dedicated lists than in general lists, adherence to the random biopsy protocol in general was poor, especially in long-segment BE. This is even more remarkable because all endoscopists were aware of the fact that they participated in a prospective study and that their performance would be analyzed. This, taken together with the tendency toward too short surveillance intervals, especially for the short BE segments, underscores the need for education of general endoscopists to improve guideline adherence.

To the best of our knowledge, this is the largest prospective study evaluating the effect of dedicated BE endoscopy lists on BE surveillance care. Data were collected prospectively in a standardized format, with few missing data. Other strengths of our study include revision of all dysplastic cases by expert pathologists, and the multivariable mixed-model analyses to account for multilevel data and possible confounding factors.

The main limitation of this study is its non-randomized design. We aimed to compensate for this shortcoming by our well-considered inclusion and exclusion criteria and multivariable analyses in which we could correct for possible confounding factors. In addition, our definition of random four-quadrant biopsy protocol adherence could be seen as lenient, as according to our definition of only one biopsy per 2 cm of BE tongues as sufficient. We deemed this as the absolute minimum number of biopsies that should be obtained. Next, in some hospitals, the BE surveillance intervals could unintentionally have been prolonged due to the COVID-19 pandemic in which surveillance endoscopies were postponed, although this applied to endoscopic services in all participating hospitals irrespective of type of endoscopy list (i. e. general list or dedicated list). Finally, no reliable data were available on the use of virtual chromoendoscopy. However, if virtual chromoendoscopy were used more regularly during dedicated BE endoscopies, that should be seen as a characteristic of dedicated BE lists rather than confounding.

Conclusions

Given the results of our study, we can conclude that clustering of BE surveillance endoscopies on dedicated lists has the potential to improve BE surveillance care by enhancing guideline adherence. Improved adherence to the four-quadrant biopsy protocol and surveillance interval recommendations might potentially result in less oversurveillance of short-segment BE and increased detection of dysplasia at an early stage.

▶ **Table 4** Characteristics of the previous BE surveillance endoscopy prior to HGD- or EAC diagnosis

Patient	Endoscopy list	Diagnosis	Previous BE length (Prague classification)	Surveillance interval (years)	Previous histology	No. biopsies previous endoscopy	Adherence biopsy protocol during previous endoscopy*	Final histological diagnosis	Final treatment
1	General list	EAC	C0M4	3.1	No dysplasia	4	Yes	T1BN1	Surgery
2	General list	EAC	C8M8	3.3	No dysplasia	11	No	T1Am3†	ESD + Surgery
3	General list	EAC	C3M3	3.2	No dysplasia	3	No	T1Am2	EMR + RFA
4	General list	EAC	C7M9	4.9	No dysplasia	3	No	T1Am3	ESD
5	General list	EAC	NR	16.0	NR	3	NR	T1Am3	EMR + RFA
6	General list	EAC	NR	15.9	NR	NR	NR	T2N1	Surgery
7	General list	EAC	C1M4	3.4	No dysplasia	4	No	T1Am3	EMR + cryoablation
8	General list	EAC	C2M3	4.1	No dysplasia	5	Yes	T1Bsm2	ESD + Surgery
9	General list	EAC	C1M2	5.3	No dysplasia	4	No	LGD	EMR + cryoablation
10	General list	EAC	C2M5	3.1	No dysplasia	12	Yes	T3N0M1	Palliative chemoradiation
11	General list	HGD	C4M4	5.2	Indefinite	4	No	T1Am2	EMR + RFA
12	General list	HGD	C0M2	0.3	Indefinite	1	Yes	HGD	EMR
13	General list	HGD	C6M6	3.0	No dysplasia	9	No	NA	NA§
14	General list	HGD	C6M7	3.2	No dysplasia	12	No	T1Am3	EMR + RFA
15	General list	HGD	C2M2	5.2	No dysplasia	5	Yes	HGD	EMR + RFA
16	General list	HGD	C8M8	2.3	No dysplasia	6	No	T1Bsm3	EMR‡
17	General list	HGD	C3M5	3.3	No dysplasia	9	Yes	HGD	EMR + cryoablation
18	General list	HGD	C1M7	1.4	No dysplasia	12	Yes	NA	NA§
19	General list	HGD	C5M6	4.2	No dysplasia	12	Yes	T1Am3	EMR
20	General list	HGD	C6M7	3.2	No dysplasia	14	Yes	T1Am3	EMR + RFA
21	General list	HGD	C12M16	0.6	No dysplasia	6	No	T1Am3	EMR
22	General list	HGD	C3M6	3.5	No dysplasia	4	No	T1Am3†	EMR + Surgery
23	General list	HGD	C3M5	2.3	No dysplasia	5	No	T1Am3	EMR + RFA
24	Dedicated BE list	HGD	C3M4	3.4	No dysplasia	12	Yes	HGD	EMR + RFA
25	Dedicated BE list	HGD	C2M4	0.7	No dysplasia	9	Yes	No dysplasia	EMR
26	Dedicated BE list	HGD	C4M6	3.7	No dysplasia	5	No	T1Am3	EMR + RFA

▶ **Table 4** (Continuation)

*Adherence was defined as four-quadrant random biopsies every 2 cm of circumferential BE extent, plus at least one biopsy every 2 cm of BE tongues. In the presence of visible lesions, target biopsies and random biopsies were summed.
†Poorly differentiated.
‡Refrained from additional surgery, patient preference.
§No additional treatment due to patient comorbidities and/or patient preference.
BE, Barrett's esophagus; EAC, esophageal adenocarcinoma; EMR, endoscopic mucosal resection; ESD, endoscopic submucosal dissection; HGD, high-grade dysplasia; LGD, low-grade dysplasia; NR, not reported; NA, not applicable; T1Am2, invasion in lamina propria; T1Am3, invasion in muscularis mucosae; T1Bsm2, submucosal invasion > 500 µm and ≤ 1000µm; T1Bsm3, submucosal invasion > 1000 µm; T1BN1, submucosal cancer with regional lymph node metastasis; T2N1, cancer invading the muscularis propria with regional lymph node metastasis; T3N0M1, cancer invading the adventitia with distant metastasis.

▶ **Table 5** Crude and multivariable analyses for random biopsy protocol adherence, surveillance interval adherence and dysplasia detection in relation to dedicated BE endoscopy lists using general endoscopy lists as reference group.

	Univariable OR	95% CI	Multivariable OR	95% CI
Random biopsy protocol adherence				
General endoscopy lists	1.00	ref	1.00	ref
Dedicated BE lists	3.43	1.77–7.21	4.45*	2.07–9.57
Surveillance interval adherence				
General endoscopy lists	1.00	ref	1.00	ref
Dedicated BE lists	1.75	1.12–2.78	1.64†	1.03–2.61
Total dysplasia detection				
General endoscopy lists	1.00	ref	1.00	ref
Dedicated BE lists	1.05	0.61–1.82	0.96‡	0.53–1.70
HGD/EAC detection				
General endoscopy lists	1.00	ref	1.00	ref
Dedicated BE lists	0.37	0.09–1.17	0.49‡	0.14–1.76

*Corrected for age, gender, ASA-score, time since baseline endoscopy, use of sedation, BE length, use of acetic acid chromoendoscopy, visible abnormalities.
†Corrected for age, gender, ASA-score, time since baseline endoscopy.
‡Corrected for age, gender, ASA-score, time since baseline endoscopy, use of sedation, BE length, use of acetic acid chromoendoscopy.
ASA, American Society of Anesthesiologists; BE, Barrett's esophagus; CI, confidence interval; EAC, esophageal adenocarcinoma; HGD, high-grade dysplasia; OR, odds ratio.

Conflict of Interest

The authors declare that they have no conflict of interest.

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