Biomarker Risk Stratification Using the Capsule Sponge for the Surveillance of Barrett's Esophagus: Interim Results from UK real-world implementation pilots.

Introduction

Endoscopic surveillance is recommended for Barrett's esophagus (BE), but the effectiveness is questionable. We previously developed a simple risk score for capsule-sponge surveillance comprising: low (clinical and sponge biomarkers negative), moderate (positive clinical biomarkers, negative sponge biomarkers), and high-risk (positive sponge biomarkers, i.e. atypia or atypia of uncertain significance (AUS), or p53 positive) to triage patients for their next endoscopy (*Pilonis et al*). Here, we prospectively evaluate the accuracy of the risk stratification tool in patients undergoing BE surveillance.

Methods

BE patients undergoing capsule-sponge at 5 hospitals within the DELTA (Jan 2020-2022, ISRCTN91655550) and NHS England (Jan 2022-ongoing) implementation studies with endoscopic follow-up were included. All samples were processed in a centralised, accredited laboratory and positive biomarkers were confirmed by 2 pathologists. The responsible clinician determined endoscopic follow-up intervals informed by the risk group – urgent endoscopy in high risk versus delayed endoscopy in low and moderate risk scheduled according to clinician's discretion. The primary outcome was the PPV and NPV for detecting dysplasia according to the risk groups. The secondary outcome was the PPV for different sponge biomarker combinations among the high-risk group (atypia, atypia uncertain significance (AUS), p53) for a diagnosis of dysplasia. Dysplasia in low and moderate-risk groups was classified according to prevalent (≤12 months) and incident (>12 months).

Results

Of 326 patients, the category breakdown was 172 (52.8%) low; 93 (28.5%) moderate, and 61 (18.7%) high risk. The PPV of the high-risk category for dysplasia was 44.3% (27/61) (13 LGD or crypt dysplasia, 10 HGD, 3 intramucosal, 1 adenocarcinoma) Within the high-risk category the PPV for dysplasia when p53 and atypia were positive was 92.8% (13/14), compared to 50% when either atypia (1/2) or p53 (4/8), were positive; whereas AUS included inflammatory changes and had less predictive potential with a PPV for dysplasia of 19.4% (6/31). The NPV for dysplasia in low-risk patients was 98.3% (169/172), with 1.7% (3/172) having dysplasia (1 LGD, 1 crypt dysplasia, 1 HGD) after a mean of 351 days of follow-up. The NPV of a moderate risk for dysplasia was 96.8% (90/93) with 3.2% (3/93) having dysplasia (2 LGD and 1 HGD). There were no cases of intramucosal/invasive cancer in the low and moderate-risk groups (**Table 1**).

Conclusion

A clinically applicable risk panel provides accurate stratification in a real-world BE surveillance setting. This simple capsule-sponge procedure has the potential as a less operator-dependent, cost-effective, and patient-friendly triage to help prioritise endoscopy requirements.

Table 1. Demographics and Histologic Outcomes by Risk Stratification Category

Parameter	Low Risk[%] (n=172)	Moderate Risk[$] (n=93)	High Risk[£] (n=61)
Age, mean (SD)	65.8 (10.2)	66.3 (14.8)	69.3 (8.0)
Gender			
- Males	134 (77.9)	66 (71.0)	45 (73.8)
- Females	38 (22.1)	27 (29.0)	16 (26.2)
BE length, cm (median, IQR)			
- Circumferential length	0 (1)	4 (4)	1 (4)
- Maximum length	2 (1)	6 (3)	4 (4)
Histopathology, n (%)			
- Non-dysplastic*	169 (98.3)	90 (96.8)	34 (55.7)
- Low-grade or crypt dysplasia	2 (1.2)	2 (2.2)	13 (21.3)
- High-grade dysplasia	1 (0.6)	1 (1.1)	10 (16.4)
- Intramucosal carcinoma	0	0	3 (4.9)
- Adenocarcinoma	0	0	1 (1.6)
Dysplasia, n			
- Prevalent (<12 months from capsule-sponge)	1	0	27
- Incident (>12 months)	2	3	n/a
Predictive value, n (%)			
- NPV of low risk for no dysplasia	98.3 (169/172)	-	-
- NPV of moderate risk for no dysplasia	-	96.8 (90/93)	-
- PPV of high risk for a diagnosis of dysplasia	-	-	27 (44.3)

SD, standard deviation; IQR, interquartile range; NPV, negative predictive value; PPV, positive predictive value; NDBE, non-dysplastic BE

*Includes indefinite for dysplasia

[£] High risk: positive for p53 immunohistochemistry or presence of atypia (amounting to dysplasia or uncertain significance) on sponge microscopy.

[$] Moderate risk: presence of clinical risk factors: 1) M>10 or C>6; 2) M>5 or C≥3 and Male; or 3) M>5 and C≥3 and age >60

[%] Low risk: negative sponge biomarkers and no clinical risk factors.