oesophageal changes. A diagnosis can only be made when a dense eosinophilia is confirmed on histology in the context of typical symptoms (e.g.solid food dysphagia)[1].We prospectively assessed the prevalence of EO in patients presenting to endoscopy at a tertiary referral centre with solid food dysphagia over 2 years.

Methods Between Jan 2010 and Dec 2011,746 patients with dysphagia (including food bolus obstruction)had high definition white light endoscopy performed. Patient demographics,symptomatology ,endoscopic and histological findings were recorded.EO was defined as the presence of > 15 eosinophils per high power field

Results Patients with oesophageal malignancy (n = 65),barrett's oesophagus(n = 48) and post-oesophageal surgery complications (n = 16) were excluded. Of the 628 remaining patients,388(62%) (254 male; mean age 59; range 18–88) had mid-oesophageal biopsies taken.23/388 (5.9%)were diagnosed with EO 19 male; mean age 40; range 26–56).Endoscopy showed mucosal pathology in 12/23 (52%) patients with confirmed EO; oesophagitis (n = 3),red furrows (n = 3),distal narrowing (n = 2),corrugated rings (n = 2),mucosal tear (n = 1) and white exudates (n = 1).250 of the remaining patients had grade A or B oesophagitis. Overall 17 patients had food bolus obstruction.11/17 patients had biopsies taken and 5/11(46%) showed histological evidence of EO.4/5 patients with bolus obstruction had distal oesophagitis on endoscopy but EO was confirmed following ≥4 mid-oesophageal biopsies. There was a trend towards those with EO having had a greater number of biopsies taken (mean 6.14; range 2–12) compared to those without EO (mean 5.02; range 2–8; p = 0.082).28% and 51% had ≤3 and ≤4 biopsies collected respectively. The mean (±SD) number of eosinophils/hpf in the EO group was 64.3 (51.3).

Conclusion Mid-oesophageal biopsies can diagnose EO in at least 1 in 16 cases of patients with unexplained solid food dysphagia. However,1/3 of patients in whom EO should have been considered (including 6 with food bolus obstruction)did not have biopsies collected.Furthermore, 1/4 had less than the recommended minimum 4 mid-oesophageal biopsies. In summary, our experience has shown that EO detection is likely to improve further if all patients with symptoms conducive with EO (e.g.solid food dysphagia) routinely trigger an EO biopsy protocol of ≥4 from the mid-oesophagus regardless of endoscopic findings.

Disclosure of Interest None Declared

REFERENCE

1. Liacouras CA, Furuta GT *et al.* Eosinophilic esophagitis: updated consensus recommendations for children and adults. J Allergy Clin Immunol 2011; 128(1):3–20 e6.

OC-027 DEFINING CANCER RISK IN BARRETT'S OESOPHAGUS USING A 90-GENE SIGNATURE

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Introduction Barrett's oesophagus (BE) has a highly variable outcome with 0.12–0.5% of patients per year progressing to oesophageal adenocarcinoma (EA). The histopathological grading of dysplasia is used to detect cancer risk in BE; however, considerable variability exists in the reporting of dysplasia. Molecular biomarkers that can detect BE patients with dysplasia would improve risk stratification in BE, enabling clinicians to focus on high risk patients requiring treatment and reduce endoscopic surveillance in the low risk group. The aim of this study was to identify and validate a gene expression signature as a biomarker that can objectively determine dysplastic status and thereby determine the risk of cancer progression.

Methods Microarray gene expression profiling was done using 59 oesophageal samples with strict consensus diagnosis by expert pathologists (21 BE with no dysplasia, 10 BE with low grade dysplasia, 13 BE with high grade dysplasia and 8 EA). This data was used to identify a gene signature that separated non-dysplastic BE from high grade dysplasia. Gene expression data from publically available datasets were used to validate the signature. An independent set of 135 fresh frozen samples covering a spectrum of dysplastic Barrett's stages and control tissue (40 BE with no dysplasia, 21 BE with low grade, 33 BE with high grade dysplasia, 32 EA and 9 duodenum) were used for validation using the high throughput 96:96 microfluidic Fluidigm® chip on the BioMark™ PCR system.

Results A set of 90 genes was identified that separated BE with no dysplasia from BE with high grade dysplasia. This 90-gene signature was able to separate the remaining untrained samples on the microarray dataset (7 non-dysplastic, 10 low grade dysplasia and 8 EA). The signature also separated non dysplastic BE samples from EA samples on 2 external published datasets ($p \leq 0.0012$). With the fresh frozen samples, the signature separated BE with no dysplasia from BE with dysplasia and EA with an area under the curve of 0.87 (95% CI, 0.80–0.93). Pathway analysis revealed that the RAN (RAs-related Nuclear protein) regulation pathway ($p < 0.0001$) was the most significant pathway in this gene set. Furthermore, MYC was found to be the most significant transcription factor regulating at least 30% of these genes ($p < 0.0001$).

Conclusion The 90 gene-expression profile can reliably identify BE samples with dysplasia and cancer. This approach has the potential to provide robust risk stratification in BE samples as it overcomes the problems with variability in the reporting of dysplasia.

Disclosure of Interest None Declared

OC-028 STATIN USE IS ASSOCIATED WITH IMPROVED SURVIVAL IN PATIENTS WITH OESOPHAGEAL CANCER: A SURVIVAL ANALYSIS USING THE UK GENERAL PRACTICE RESEARCH DATABASE AND NATIONAL CANCER REGISTRY

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Introduction Patients with oesophageal cancer (OC) commonly present with an advanced stage of disease, and are often only amenable to palliative therapies. Of the minority suitable for potentially curative surgery, up to 50% develop recurrence at one year. Statins demonstrate several anticarcinogenic properties in oesophageal adenocarcinoma (OAC) cell lines including reducing cell proliferation, stimulating apoptosis and potentially limiting metastatic potential. We investigated for the first time the hypothesis that statin use after diagnosis or post-oesophagectomy was associated with improved survival in patients with OC.

Methods Cases of OC diagnosed between 1st January 2000 and 31st December 2009 were identified from the UK General Practice Research Database (GPRD). The GPRD data was linked to the UK National Cancer Registry (NCR) to determine histological subtype. Cox proportional hazard regression analysis with time-dependent exposures, estimated the associations between statin use (versus non-users) from diagnosis and post-surgery on overall survival and disease-specific survival. Multivariate analyses were adjusted for age, gender, body mass index, diabetes mellitus, cardiovascular disease, oesophagectomy, chemotherapy, radiotherapy and ACE inhibitor use.

Results In total 4445 cases of OC were identified, of which 606 were OAC and 344 were OSCC (histology data was available for 21.4% of patients). Overall 585 (13.2%) patients underwent oesophagectomy. In total 609 (13.7%) of patients were statin users

following diagnosis and 109 (19.2%) following surgery. There were improved survival times following diagnosis for patients prescribed a statin with OC overall (HR = 0.71, 95% CI = 0.64–0.79, p < 0.001) and specifically OAC (HR = 0.58, 95% CI = 0.43–0.78, p < 0.001). Furthermore, statin use post-oesophagectomy was associated with improved survival in those with OC overall (HR = 0.66, 95% CI = 0.48–0.91, p = 0.013) and those with OAC specifically (HR = 0.58, 95% CI = 0.30–1.10, p = 0.096) with borderline significance. There were no significant effects between statin use and survival in patients with OSCC. Associations between statin use and overall survival were very similar to their effect on disease-specific survival.

Conclusion Statin use in patients with OC either after diagnosis or post-oesophagectomy is associated with improved survival. This data suggests a need for randomised controlled trials of statins in patients with OC.

Disclosure of Interest None Declared

OC-029 RADIOFREQUENCY ABLATION (RFA) CONFERS SUSTAINED BENEFIT FOR SQUAMOUS HIGH GRADE DYSPLASIA (HGD) AND EARLY SQUAMOUS CELL CARCINOMA (SCC) IN PATIENTS WHO DO NOT PROGRESS FOLLOWING FIRST TREATMENT

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Introduction Oesphageal SCC carries a poor prognosis. Squamous HGD is the precursor lesion to SCC. Risk of progression to SCC with HGD can be 65% at 5 years. RFA is a minimally invasive technique with proven efficacy for early neoplasia arising in Barrett's oesophagus. We present prospective data from 10 centres in the United Kingdom (UK) HALO registry.

Methods Superficial lesions were removed by endoscopic mucosal resection (EMR) before RFA. Treatment consisted of a single ablation at 12J/cm2. Patients were followed up 3 months after treatment with biopsies. Those with residual dysplasia underwent further RFA until 12 months when they were assessed for treatment success or failure. Recurrent dysplasia was retreated with EMR/RFA. Primary outcomes were reversal of dysplasia (CR-D) at 12 months.

Results 26 patients had RFA. Mean length mucosa ablated was 5.3 cm (1–14). 7/26 (27%) had EMR before RFA. Prior EMR did not confer benefit to outcome, nor did baseline disease length. Following first RFA, 6/26 patients (23%) progressed to invasive disease. Only one more patient progressed later in treatment course. CR-D was achieved in 50% at protocol end, mean 1.7 RFA treatments (1–4). 10/13 (77%) with successful RFA at 12 months remain disease free at most recent follow up (median 21 months). Kaplan Meier statistics show 2 years post treatment 68% patients are likely to remain in remission from dysplasia for those with successful outcome at 12 months. 5 patients (19%) required dilatations for oesophageal stricturing.

Conclusion Squamous HGD & CIS are aggressive pathologies as evidenced by the fact that 23% patients in our cohort progressed to invasive disease despite RFA. However the majority who do not progress early (13/19 patients) achieve benefit & are more likely to have a successful & durable outcome. There is limited experience in the UK with RFA in these patients. Pre RFA EMR for visible lesions is limited in our series. As a result some patients may be under staged prior to RFA which may account for the high rate of progression after first treatment.

Disclosure of Interest None Declared

OC-030 BARRETT'S EPITHELIUM SHOWS EVIDENCE OF GASTRIC AND INTESTINAL DIFFERENTIATION PROGRAMMES BUT PRESERVES THE PROLIFERATIVE AND STEM CELL ARCHITECTURE OF GASTRIC GLANDS

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Introduction The origin and development of Barrett's oesophagus has long been discussed, with three main proposals for the origin of metaplasia: from oesophageal squamous epithelium, from upward migration of cardiac glands, or from submucosal glands.

Methods In Barrett's glands we have studied the distribution of proliferative activity using Ki67 and the migration of cells in Barrett's glands from patients infused with iododeoxyuridine 7 and 11 days pre-oesophagectomy. We have localised gene expression of mucins using immunohistochemistry (IHC) and trefoil family factor (TFF) peptides using IHC and *in situ* hybridization (ISH) and the stem cell marker Lgr5 using ISH, combining this with analysis of the clonal architecture of Barrett's glands using mitochondrial DNA (mtDNA) as a clonal marker.

Results In Barrett's glands proliferation is seen mainly in the middle part of the gland and diminishes towards the surface and the base of the gland. Cells migrate in a bidirectional manner. MUC5AC and TFF1 expression are found superficially, while MUC6 and TFF2 are found at the bases of the glands, similar to the distribution seen in antral gastric glands: MUC2, staining goblet cells and columnar cells, is concentrated superficially. *Lgr5* mRNA is also found in the middle part of the glands, indicating the location of the stem cell niche. Barrett's glands are clonal, indicating derivation from a single cell, and suggesting that Barrett's stem cells have dual differentiation capacity. Gastric intestinal metaplasia, on the other hand, shows basal *Lgr5* mRNA localisation with a distribution of proliferative activity similar to intestinal crypts.

Conclusion We conclude that Barrett's glands show the proliferative and stem cell architecture, and preserve patterns of gene expression of pyloric-type gastric glands, but are maintained by unique stem cells with both gastric and intestinal differentiation capacity: we propose that Barrett's glands originate as gastric glands and that subsequent intestinal differentiation advances with time, strongly supporting an origin from the proximal cardiac mucosa.

Disclosure of Interest None Declared

OC-031 USING GENOME-WIDE STUDIES TO IDENTIFY NOVEL FOXM1 TRANSCRIPTION FACTOR TARGET GENES IN OESOPHAGEAL CANCER

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