Surprisingly in 53% of NDBE tissue samples we identified clonal expansion of cells (>10% mutant fraction) harbouring mutations in one or more of 13/15 of these putative driver genes. No difference in the frequency of mutation of these genes was observed between any of the disease stages studied. *TP53* mutations clearly delineate between HGD/OAC and benign NDBE ($p < 0.001$). Whilst *SMAD4* mutations are only observed in OAC ($p < 0.001$) demonstrating for the first time a clear genetic difference between the two.

Conclusion Mutagenic processes active in OAC are also active in the earliest stages of BE. Recurrent driver mutations identified in cancer may be acquired very early in the disease and may provide little or no progression advantage. Molecular diagnostic approaches must account for this.

Disclosure of Interest None Declared.

PTU-154 DIFFERENCES IN COELIAC SEROLOGY OUTCOMES APPEAR DEPENDANT UPON THE ORIGIN OF THE REQUEST: A SEVEN YEAR REVIEW OF ANTI-TISSUE TRANSGLUTAMINASE TESTING

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Introduction Coeliac disease is the most common genetically based food intolerance worldwide with a UK prevalence of 1 in 150. The condition poses a diagnostic difficulty due to the often non-specific symptoms at presentation and a sub-group who will be asymptomatic. Successful diagnosis is based upon a high degree of suspicion, correct screening and a subsequent confirmatory test with an intestinal biopsy. Serological testing via anti-endomysial antibody (AEA) and anti-tissue transglutaminase (ATTG) is a simple, highly accurate method of screening, with a sensitivity and specificity in the region of 95–98% and 95–97%, respectively. Due to these attributes, serological screening accounts for a significant proportion of laboratory workloads nationwide.

Methods All ATTG coeliac serology requests made in a busy district general hospital over a 7 year period between 2007 and 2013 were reviewed, with a particular focus upon the positive results. A further assessment of case records and in particular the origin of requester was conducted. A positive result was issued by the laboratory if the ATTG was greater than or equal to 4.

Results Overall, a total of 29795 ATTG requests were made to the biochemistry department, of which results were obtained from 28819. Of this number, 1005 were performed in inpatients, 7140 in outpatients and 20674 were from primary care. In the GP cohort, 785/20674 (3.8%) proved to be positive. In comparison 37/1005 (3.7%) were positive from the inpatient group, and 371/7140 (5.2%) were positive from the outpatient cohort. The deficit in results gained was primarily due to the rejection of samples by the laboratory as being "not indicated" in 402 inpatient cases (27%) and 4 outpatient cases. No GP requests were rejected. The overall numbers of ATTG requests also increased year on year with 913 being performed in 2008 and 6483 in 2013.

Conclusion It is clear the demand for coeliac serology is increasing with its use becoming more widespread in a variety of clinical settings. The mere fact that patients are presenting to hospitals for outpatient appointments or inpatient assessments, places them in a self selecting group where one would expect to see a higher frequency of positive coeliac serology. This was duly noted in our outpatient cohort, but the inpatients had a similar positive pick up rate to the GP cohort. It is possible this result was slightly skewed by the high rejection rate seen with inpatient requests. The high positive pick up rate from specialist outpatient clinics emphasises the importance of having a high degree of clinical suspicion in order to make an appropriate diagnosis.

Disclosure of Interest None Declared.

PTU-155 PROGRESSION OF LOW GRADE DYSPLASIA TO HIGH GRADE DYSPLASIA IN BARRETT'S OESOPHAGUS IN A SINGLE CENTRE

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Introduction Barrett's oesophagus is a common condition found in 4% of patients undergoing upper gastrointestinal endoscopy.(1) The association between Barrett's oesophagus and oesophageal adenocarcinoma has been well established. Scotland has a particularly high incidence of both Barrett's and adenocarcinoma of the oesophagus.

The risk of progression from high grade dysplasia (HGD) to oesophageal adenocarcinoma (OAC) has been reported at approximately 10% per year.[1] However the risk of progression from low grade dysplasia (LGD) is harder to quantify with studies showing progression to OAC from 0.6–1.69% per year, not dissimilar to that of non-dysplasic Barrett's.[2] More recently the SURF trail reported a 25% (17/68) progression from LGD to HGD/OAC in a surveillance group with LGD versus radiofrequency ablation.[3]

Methods In 2009 a clinical database of Barrett's patients was developed in Forth Valley Hospital to ensure appropriate surveillance as per BSG guidelines. All patients diagnosed with Barrett's were cared for by one responsible team, a dedicated Barrett's endoscopy list was developed, and the use of narrow band imaging was introduced. At the end of 2012 the database was interrogated to assess the progress of all patients who had been diagnosed with LGD within the previous three years.

Results There were 915 patients with Barrett's on the database, of which 829 were under follow up. 85 (10%) had LGD and of this patient cohort 19 had progressed to HGD. The progression rate from LGD to HGD was 22% (19/85). The median follow up of patients with LGD was 29 months (range 12–34 months). All patients who progressed from LGD to HGD had endoscopic therapy with endoscopic mucosal resection and /or ablative therapies. There are no recorded cases of progression of LGD to OAC.

Conclusion The progression rate from LGD to HGD is similar to reported rates found in the SURF trial. This suggests that LGD carries a greater risk of progression, and therefore worse prognosis than previously reported. This is a potential group of patients in whom to consider early intervention rather than adopt the standard surveillance strategy. Further studies to evaluate the effectiveness of treatment rather than surveillance in this group should be considered.

REFERENCES

1 Consensus Statements for Management of Barrett's Dysplasia and Early-Stage Esophageal Adenocarcinoma, Based on a Delphi Process. *Gastroenterology* 2012;143 (2):336–346

2 Sachin W, Sharad M. How to manage a Barrett's Esophagus patient with low grade dysplasia. *Clin Gastroenterol Hepatol*. 2009;7(1):27–32

3 Phoa K, von Vilstern, F. Radiofrequency Ablation in Barrett's esophagus with confirmed low-Grade dysplaisa: interm results of a European multipcentre randomized controlled trial (SURF). *Gastroenterology* 2013: 5 Supplement1 S187

Disclosure of Interest None Declared.

PTU-156 HEPATOCYTE NUCLEAR FACTOR 4 ALPHA (HNF4A) IS DEMONSTRATED IN BARRETT'S METAPLASIA, BUT NOT IN NORMAL HUMAN OESOPHAGUS

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Introduction Barrett's metaplasia (BM) is the main risk factor for oesophageal adenocarcinoma, a cancer which carries a mortality of >50% at 12 months. Refluxate containing gastric and bile acids seems to be causative for inflammation at the lower oesophagus, but it is not known how this induces replacement of stratified squamous epithelium (SSQE) with columnar epithelium at a molecular level.

There is likely to be a progenitor cell population replacing denuded epithelium, although the origin of these cells has not been proven. Genes that play a role in gut tissue patterning during embryogenesis have received attention. One such 'master switch' our laboratory is investigating encodes the hepatocyte nuclear factor 4 alpha (HNF4α) transcription factor.

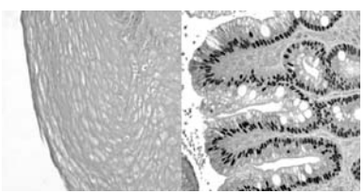
Methods We optimised an immunohistochemistry protocol for demonstrating HFN4α on formalin-fixed paraffin-embedded slides of human tissue. This protocol was applied to forceps biopsy specimens of normal oesophagus, gastro-oesophageal junction (GOJ), stomach, ileum, colon and BM (UK REC reference: 13/YH/0197). Tissues were examined from at least 3 different patients per anatomical site.

Results In healthy tissues, nuclear HNF4α positive immunostaining was demonstrated in stomach, ileum and colonic epithelium, but not in normal SSQE in the oesophagus. At the GOJ, there was clear delineation between HNF4α positive nuclei in the columnar gastric cardia mucosa, and negative HNF4α staining of SSQE. In contrast, the columnar epithelial nuclei in BM were consistently positive.

Conclusion HNF4α transcription factor is demonstrable in BM, but not SSQE. We are not aware that this HNF4α gastrointestinal distribution has been previously published. HNF4α is likely to be a key transcription factor in the pathogenesis of BM.

Previous work in our laboratory with a mouse explant tissue culture model has shown that another candidate transcription factor responsible for BM (Cdx2) was insufficient to induce an intestinal phenotype, whereas HNF4α induced villin, K18, trefoil factor 3 and mucin 5AC. We propose a 2-hit hypothesis for the development of BM:

1. induction of HNF4α (which initially converts the oesophageal SSQE to columnar epithelium) and
2. Cdx2 (which causes intestinalisation of the columnar epithelium).



Abstract PTU-156 Figure 1

Demonstration of HNF4α in BM but not SSQE is supportive of this theory.

Disclosure of Interest None Declared.

PTU-157 OUTCOMES OF OESOPHAGEAL DILATATION IN ACHALASIA AND POST-FUNDOPLICATION DYSPHAGIA

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Introduction Dilatation of the Oesophago-Gastric Junction (OGJ) provides effective symptom relief in 58–95% of patients with achalasia, similar to that achieved by Heller's myotomy. Dilatation is also used in patients with persistent (>6 months) dysphagia after fundoplication surgery; there is insufficient safety and outcome data of this procedure. Our aim is to compare patient outcome of endoscopic dilatation for both these conditions.

Methods We present 18 month experience of referrals to the dysphagia service 2012–2013. All patients underwent a diagnostic gastroscopy with biopsies, excluding inflammation or neoplasia. Patients with achalasia or clinically relevant outlet obstruction post-fundoplication diagnosed by elevated integrated relaxation pressure (>25 mmHg) on high resolution manometry were selected. Dilatation was performed by 30–35mm Rigiflex II Balloon or Savary-Gillard Bougies (max 18mm) under fluoroscopic guidance. Primary outcome was symptom response at 3–6 months post-procedure by clinic or telephone follow-up. Overall symptom response was documented on an analogue scale from 0% >100% (inadequate <40%, satisfactory 40–60%, good 60–80% and excellent >80%).

Results 46/71 referrals had either achalasia or dysphagia post fundoplication. 30 (41%) had achalasia, 6 had prior Heller's myotomy and 7 had prior Botulinum toxin. 16 (22%) patients had OGJ obstruction after fundoplication. 29/30 patients with achalasia underwent pneumatic dilatation, one bougie dilatation. Overall symptom response was inadequate in 5 (16% referred for surgery), satisfactory in 3 (11%) and good-excellent in 22 (73%).14/16 patients with post fundoplication dysphagia had pneumatic balloon dilatation, 2 had bougie dilatation. Overall symptom response was inadequate in 7 (44% referred for surgery), satisfactory in 4 (25%) and good-excellent in 5 (31%). Complications from the both groups include chest pain (n = 2), chest infection (n = 1), reflux symptoms (n = 4 in each group) and minor bleeding. All resolved with conservative treatment.

More than half of achalasia and post-fundoplication patients reported "at least satisfactory" outcome 3–6 months after dilatation (84% vs. 56%; $p < 0.07$ Fisher Exact Test). A good-excellent symptom response was reported more often by achalasia patients ($p = 0.010$).

Conclusion Endoscopic dilatation is safe and effective treatment for patients with dysphagia related to achalasia and also OGJ obstruction post-fundoplication. A good-excellent response was reported less frequently by the post-fundoplication patients; however more than half had at least "satisfactory" symptom relief and, therefore, a trial of endoscopic dilatation can be considered a viable alternative to re-operation.

Disclosure of Interest None Declared.