Surprisingly in 53% of NDBE tissue samples we identified clonal expansion of cells (>10% mutant fraction) harbouring mutations in one or more of 13 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-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 3
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 4 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.5 More recently the SURF trial reported a 25% (17/68) progression from LGD to HGD/OAC in a surveillance group with LGD versus radiofrequency ablation.

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
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 HNF4α 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).

**Disclosure of Interest** None Declared.

**PTU-157**

**OUTCOMES OF OESOPHAEGAL DILATATION IN ACHALASIA AND POST-FUNDOPLICATION DYSPHAGIA**


10.1136/gutjnl-2014-307263.231

**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 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.