Overall, seven of these specimens contained both mutated and wild type dysplastic glands, with a further one specimen containing three distinct p16*INK4A*mutation. However, the related cancers from these specimens were monoclonal for a mutated genotype found in the dysplasia. These data show that Barrett's dysplasia is polyclonal but Barrett's adenocarcinoma is monoclonal, suggesting that a cellular competition may be involved in the evolution of Barrett's adenocarcinoma from its surrounding dysplasia.

Conclusion

1. Barrett's dysplasia exhibits a mosaic pattern of clones, indicating genetic diversity in Barrett's dysplasia.
2. Oesophageal adenocarcinomas were monoclonal outgrowths from polyclonal Barrett's dysplasia.

Competing interests None declared.

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OC-085 CIRCULATING TUMOUR MARKERS CAN DISCRIMINATE BETWEEN PATIENTS WITH AND WITHOUT OESOPHAGEAL NEOPLASIA

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Introduction Oesophageal cancer is the fastest rising cause of gastrointestinal cancer in the UK, and associated with a poor prognosis. Early diagnosis represents the best opportunity for cure, but early disease is often asymptomatic. Current surveillance programs improve outcome, but rely on two yearly endoscopic screening of previously identified Barrett's oesophagus patients. This has limited sensitivity and acceptability to patients. New endoscopic treatments for oesophageal dysplasia can avoid major surgery, but discriminating between patients with and without invasive disease can be challenging. A discriminating diagnostic blood test may offer improved patient outcome.

Methods In this study, we optimised a series of promising diagnostic markers utilising circulating free DNA (cfDNA), with a preparation method allowing small DNA fragments to be purified. cfDNA was isolated from 115 patients including a "normal" population of 44 patients (Barrett's oesophagus or normal endoscopic findings). Twenty-five patients had high grade dysplasia (HGD) or intramucosal cancer (IMC), and 46 patients had invasive cancer. In each case real time quantitative polymerase chain reaction (RT-PCR) was performed for Line 1 79 bp (quantitative total DNA marker), Line 1 300 bp, Alu 115 bp, Alu 247 bp and mitochondrial primers. Each marker was analysed for differences between normal, HGD and IMC, and invasive cancer populations using Mann–Whitney U tests and ROC curves. The best performing were analysed in combination by logistic regression. A Bonferroni correction was applied.

Results The average age of the normal population group was 56.1 years, the HGD and IMC population group 70.0 years, and the cancer population group 68.9 years. The mean total DNA (ng/ml) was 10.8, 14.1, and 19.2 respectively. Mean DNA marker levels ng/ml. Analysing total DNA, mitochondrial DNA and Line 1 300bp fragment DNA levels, there were highly significant differences between the normal group vs all dysplastic and cancerous patients ($p \leq 0.003$).

Conclusion The combination DNA marker was able to discriminate the normal population from all dysplasia and cancer patients with a ROC curve of 0.778. This may offer the prospect of a simple blood test to stratify patients and improve surveillance for dysplasia and early cancer. The same model was able to discriminate the normal population from invasive cancer patients with a ROC curve of 0.847. This may help in the rapid identification of patients who require surgery.

Abstract OC-085 Table 1

Mean DNA	Total	Mito	115	300	247	79/300	115/247
"Normal"	10.8	1.1	35.6	1.8	3.1	6.3	11.0
HGD + IMC	14.1	4.2	42.6	3.2	4.6	6.1	10.3
Inv. cancer	19.2	6.2	76.9	5.3	4.9	8.8	16.3

Competing interests None declared.

OC-086 SURGERY ALONE VS CHEMORADIOTHERAPY FOLLOWED BY SURGERY FOR STAGE I AND II OESOPHAGEAL CANCER: FINAL ANALYSIS OF A RANDOMISED CONTROLLED PHASE III TRIAL—FFCD 9901

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Introduction Resection remains the best treatment for local control of oesophageal carcinoma (OC), but local recurrence, distant metastasis and poor survival remain an issue after surgery. Often investigated in locally advanced OC, the impact of neoadjuvant chemoradiotherapy (NCRT) is unknown in patients with stage I or II OC. The aim of this multicentre randomised controlled phase III trial was to assess whether NCRT improves outcomes for patients with stage I or II OC.

Methods 195 patients were randomly assigned to surgery alone (S group, n=98) or to NCRT group (NCRT group, n=97; 45Gy given in 25 fractions over 5 weeks with two courses of concomitant chemotherapy by 5-Fluorouracil 800 mg/m^2 on days 1–4 and cisplatin 75 mg/m^2 on day 1 or 2). The primary endpoint was overall survival. Secondary endpoints were progression free survival, postoperative morbidity and 30-day mortality, R0 resection rate and prognostic factor identification. Analysis was done by intention to treat.

Results Patient and tumour characteristics were well-balanced between the two groups. Patients were preoperatively staged I in 18%, IIA in 49.7%, IIB in 31.8%, unknown in 0.5%. Postoperative morbidity and 30-day mortality rates were 49.5% vs 43.9% (p=0.17) and 1.1% vs 7.3% (p=0.054) in the S group and NCRT group, respectively. After a median follow-up of 5.7 years, 106 deaths were observed. Median survivals were 43.8 vs 31.8 months, respectively (HR 0.92, 95% CI 0.63 to 1.34, p=0.66). The trial was stopped due to futility.

Conclusion Compared with surgery alone, NCRT with cisplatin and 5-Fluorouracil does not improve overall survival but enhances postoperative mortality for patients with stage I or II OC (Clinical Trial.gov identifier NCT 00047112).

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Competing interests None declared.

OC-087 CLINICAL EVALUATION OF OESOPHAGEAL MUCOSAL INTEGRITY AND ACID SENSITIVITY IN PATIENTS WITH NERD. A STUDY USING BASAL IMPEDANCE AND ASSESSMENT OF MUCOSAL RECOVERY AFTER ACID CHALLENGE

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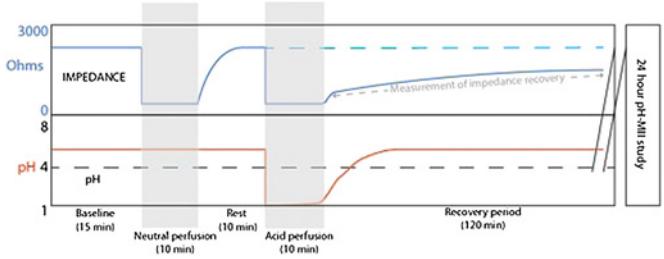
Introduction Patients with NERD have no erosions but impaired oesophageal mucosal integrity, that is, dilated intercellular spaces. It has been proposed that such microscopic changes can underlie symptoms in NERD, however, the relationship between impaired mucosal integrity and acid perception is unclear. Thus far, oesophageal mucosal integrity has been studied in vitro. Recently, oesophageal impedance basal values have been suggested as an in vivo surrogate to assess mucosal integrity in man. Low basal impedance is seen in patients with higher oesophageal acid exposure, and improves after PPI treatment. Oesophageal mucosal integrity, as expressed by basal impedance, is probably a dynamic process reflecting (1) the damaging effect of repeated acid reflux events and (2) the mucosal capacity to recover integrity. We hypothesised that there may be a relationship between mucosal integrity, recovery capacity and acid perception. We **aimed** to study the relationship between the dynamic properties of oesophageal mucosal integrity after acid challenge and symptom perception in patients with reflux symptoms.

Methods We studied 53 patients with typical reflux symptoms and no oesophagitis. A combined pH-MII catheter was inserted, and baseline distal oesophageal mucosal impedance measured for 15 min (and continuously thereafter). We performed a 10 min mid-oesophageal perfusion (10 ml/min) of a neutral solution. After a 10 min rest period an acid perfusion was performed with pH1 solution. Symptoms were recorded with a visual analogue scale. Impedance recovery was observed for 2 h post-acid perfusion in ambulatory conditions. Subjects then completed a 24 h reflux study.

Results There was significant inter-individual variability in pre-perfusion impedance baselines (mean 2059Ω, range 462–5388). Neutral perfusion caused a drop in impedance that recovered fully in 10 min. Acid perfusion caused a drop in impedance that was slow to recover. The mean impedance recovery rate was 7.5 Ω/min (25th–75th percentile=3.1–10.9). 32 of 53 patients perceived heartburn during acid perfusion. Patients with slower impedance recovery (<25th percentile, n=12) had lower basal impedance (mean±SEM 1331Ω±256 vs 3325Ω±325, p<0.01), higher 24 h acid exposure (5.2%±1.0 vs 1.7%±0.3, p<0.01), and more often acid sensitivity (10/12 vs 5/13, p<0.05) than those with faster impedance recovery (>75th percentile, n=13).

Conclusion A continuous impaired mucosal integrity (low impedance) might be a consequence of repeated reflux episodes with slow recovery. There is a link between mucosal integrity, recovery capacity and symptom perception. Low basal impedance and slow recovery after acid challenge are associated with increased acid sensitivity.



Abstract OC-087 Figure 1

Competing interests None declared.

OC-088 IGE SENSITISATION TO FOOD AND INHALANT ALLERGENS IN UK ADULTS WITH EOE: A PILOT STUDY

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Introduction Food and inhalant allergens have been implicated as triggers of eosinophilic oesophagitis (EoE). Although topical steroid therapy remains the mainstay of treatment in adults, elemental and six food elimination diets have been shown to decrease oesophageal eosinophilia and improve symptoms in children and more recently in adults. Limited data in North American adult EoE patients suggests that food allergens commonly associated with IgE sensitisation are peanut, egg and soy. We hypothesised that IgE sensitisation to foods and/or cross-reactive inhalant allergens plays a role in EoE. To test the hypothesis we designed a pilot study to explore possible relationships between IgE sensitisation to food/inhalant allergens and EoE in a UK adult population.

Methods Ten adult patients with biopsy-proven EoE (>15 eosinophils/HPF) but no previously documented food allergy were included. Participants completed food allergy and dysphagia questionnaires, and underwent skin prick testing (SPT) to a battery of inhalant allergens: timothy grass, birch, six grasses, three trees, plane, mugwort, ragweed, *Alternaria*, *Cladosporium*, *Aspergillus*, house dust mite (HDM) and latex. Foods tested were milk, egg, prawn and cod and plant-derived foods: peanut, hazelnut, sesame, soy, mustard, corn, wheat, barley, celery, raw potato, apple, peach, grape, orange, tomato, melon, kiwi and strawberry. All SPT's were performed in the presence of positive (histamine) and negative (saline) controls. A wheal size 3 mm or more than the negative control was considered positive.

Results Of the 10 subjects (7 m, median age 33 years, range 26–52) who completed the study, eight reported dysphagia to solids nine times or more in the previous month. Two patients had required hospital admission in the previous month. Nine subjects identified one or more specific foods as a trigger for symptoms. The most commonly cited foods that were thought to trigger symptoms were meat (lamb or chicken) in four, nuts in three and citrus fruits or apples in three. Nine subjects had positive skin tests to both grass pollen and HDM; four of these subjects also had positive tests to at least three other inhalant allergens. These four subjects had the highest number of positive skin tests to foods (median of 9).The most common positive food SPTs were barley (7), wheat (5) and potato (4).

Conclusion The high prevalence of IgE sensitisation to foods in this pilot study supports our hypothesis that this plays a role in adult EoE pathophysiology. The high rates of barley and wheat sensitisation raise the possibility of IgE crossreactivity with homologous plant allergens in EoE, notably grass pollen. Further larger studies