treatment plan included neoadjuvant CRT (cisplatin + 5-Fluorouracil/45 Gy) followed 6–8 weeks later by a transthoracic en bloc oesophagectomy. Morphological evaluations combined with FDG-PET results were performed 2 weeks before and 4–6 weeks after the completion of CRT. Intratumoural pre- and post-treatment FDG-standardised uptake values were assessed (SUV1, SUV2, percentage change). These variables were correlated with pathologic and morphologic responses and survival. Investigators were blinded to the FDG-PET results unless metastatic disease was suspected.

Results Out of 60 total patients, 46 underwent the complete treatment plan (median age: 60.1 years; adenocarcinoma: 25 patients; squamous cell cancer: 21 patients). A major pathological response occurred in 19.6% of patients and was associated with a favourable outcome ($p=0.057$). Neoadjuvant CRT led to a significant reduction in intratumoural FDG-uptake ($p<0.001$). No significant association was seen between a pathologic response (either complete or major) and the FDG-PET results ($p>0.280$). The SUV2 value was correlated with a morphological response and the possibility to perform an R0 resection ($p<0.018$; ROC analysis: SUV2 threshold = 5.5). No significant association was found between metabolic imaging and recurrence or survival.

Conclusion FDG-PET does not effectively correlate with pathologic response and long-term survival in patients with locally advanced oesophageal cancer undergoing neoadjuvant CRT followed by surgery (registered on <http://www.e-cancer.fr> website, RECF0350, 2002-1936R).

Funding Funded by the French ministry of Health — Programme Hospitalier de Recherche Clinique 2002.

Competing interests None declared.

PTU-184 DEFINING AND TREATING A POSITIVE CIRCUMFERENTIAL RESECTION MARGIN IN OESOPHAGEAL AND GASTRO-OESOPHAGEAL JUNCTIONAL CANCER

doi:10.1136/gutjnl-2012-302514c.184

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Introduction A positive circumferential resection margin (CRM) has been implicated with poorer prognosis in oesophageal and gastro-oesophageal junctional (OGJ) cancer. The Royal College of Pathologists (RCP) defines a margin as positive if tumour cells are present within 1 mm. In contrast, the College of American Pathologists (CAP) only defines a margin as positive if tumour cells are observed at the margin. The equivalence of the systems is not clear and the impact of adjuvant treatment has not been assessed.

Aims To compare the prognostic ability of the RCP and CAP systems in a cohort from a single UK centre and to determine if adjuvant radiotherapy offers a survival benefit for CRM positive patients.

Methods Patients with a "T3" adenocarcinoma or squamous cell carcinoma of the oesophagus or OGJ undergoing potentially curative resection between 1994 and 2010 were identified from a prospective database. Resection specimens were reviewed and the CRM was measured to ± 0.1 mm by a consultant pathologist. Univariate, multivariate and propensity score matching analyses (PSMA) were performed.

Results A total of 226 patients were included. Cox regression demonstrated patient sex ($p=0.009$), tumour differentiation ($p=0.015$), nodal (N) stage ($p<0.001$) and CRM group ($p=0.045$) were independently predictive of prognosis. Patients were grouped into CRM of 0 mm (CAP+ve, $n=47$), CRM >0 mm but <1 mm

(RCPCRM, $n=83$) and CRM ≥ 1 mm (CRM-ve, $n=96$). Median survivals (95% CIs) were significantly different across groups ($p=0.019$) with CAP+ve = 18 months (13.0 to 23.0), RCPCRM = 28 months (18.6 to 37.3) and CRM-ve = 33 months (25.8 to 40.2). A trend for poorer survival was noted for the CAP+ve vs the RCPCRM group ($p=0.073$) although there was heterogeneity in N stage across groups. PSMA demonstrated no residual survival difference between CAP+ve and RCPCRM groups when other prognostic variables were controlled. Significant selection bias was observed for patients undergoing adjuvant radiotherapy. PSMA was applied to assess the treatment effect. Patients undergoing adjuvant radiotherapy ($n=23$) showed significantly improved survival when compared to controls ($n=23$) matched for sex, pre-operative treatment, N stage, histology and differentiation ($p=0.04$).

Conclusion The survival difference between CAP+ve and RCPCRM groups could be explained by existing prognostic variables. The CAP and RCP systems therefore appear equivalent in our cohort. In selected patients with a CRM <1 mm, adjuvant radiotherapy may be of benefit and a prospective randomised trial is indicated.

Competing interests None declared.

PTU-185 NOVEL TECHNIQUES FOR ASSESSING OESOPHAGO-PHARYNGEAL REFLUX IN PATIENTS WITH HOARSENESS AND SUSPECTED LARYNGOPHARYNGEAL REFLUX

doi:10.1136/gutjnl-2012-302514c.185

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Introduction It is suggested that hoarseness along with typical signs on laryngoscopy can be caused by oesophago-pharyngeal reflux, often referred to as LPR. New methods are proposed to assess pharyngeal exposure to gastric contents. They are suggested to measure (1) liquid or mixed gas-liquid acid and non-acid reflux (HMII-pH), (2) aerosolized acid reflux (Dx-pH measuring system, Restech), and (3) presence of pepsin in saliva. We aimed to quantify pharyngeal exposure to gastric contents in patients with hoarseness and healthy controls using the above techniques.

Methods 21 patients with hoarseness and a positive laryngoscopy (mean age: 51 range: 23–75) and 10 asymptomatic controls (mean age: 26, range: 21–34) underwent simultaneous HMII-pH monitoring, oropharyngeal pH monitoring and saliva pepsin sampling. The HMII-pH catheter was located with impedance sensors in the oesophageal body, 3–5 cm distal and 0–2 cm proximal to the UOS. The Dx-pH catheter was located posterior to the uvula and pepsin in saliva was measured using an in vitro device utilising two pepsin monoclonal antibodies (PepTest) at five different times during the 24-h period. Patients were studied "off" PPI.

Results Healthy controls had (1) no liquid or mixed gas/liquid reflux in the pharynx, (2) two controls had +ve Dx-pH and (3) two controls had more than one saliva sample +ve for pepsin with the other tests negative. Patients were classified into four groups: (a) all tests +ve ($n=2$); (b) two tests +ve (MII-pH + pepsin ($n=5$) or MII-pH + Dx-pH ($n=3$); (c) all tests negative ($n=5$) and (d) patients with +ve Dx-pH or pepsin without evidence of HMII detected reflux. These patients were considered negative ($n=6$). Dx-pH drops were poorly associated with HMII-pH reflux. 11% of Dx-pH drops to $pH<4$, 15% of pH drops to $pH<5$ and 10% of pH drops to $pH<5.5$ coincided with HMII detected liquid or gas reflux in the oesophageal body. The detection of pepsin in saliva occurred in 7/10 patients with acid or non-acid HMII detected reflux. Positive pepsin saliva samples were preceded by more reflux events in the previous 60 min 3 (1–4) than negative samples 0 (0–2) $p<0.0001$.

Conclusion We identified a subgroup of patients with hoarseness with objective detection of oesophago-pharyngeal reflux (10/21). (b) the majority of oropharyngeal pH drops detected by Dx-pH do not correlate with retrograde flow (liquid or gas) in the oesophageal body. (c) Detection of pepsin in saliva suggests the likelihood of reflux episodes in the previous 60 min.

Competing interests None declared.

PTU-186 EXOGENOUS NSAID EXPOSURE INCREASES TRANSCRIPTIONAL EXPRESSION OF THE 5-LIPOXYGENASE PATHWAY IN NORMAL SQUAMOUS TISSUE, BUT NOT IN BARRETT'S METAPLASIA: AN EX VIVO STUDY OF OESOPHAGEAL BIOPSY SPECIMENS

doi:10.1136/gutjnl-2012-302514c.186

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Introduction Barrett's oesophagus (BO) is a premalignant condition for oesophageal adenocarcinoma, an increasingly common malignancy with poor survival. The prostanoids and leukotrienes are lipid inflammatory mediators derived from a common precursor by the cyclooxygenase (COX) and 5-lipoxygenase (5-LO) pathways respectively. Both families have been implicated in oesophageal adenocarcinoma, prompting studies of the effects on disease progression of drugs that modulate these pathways. NSAIDs may prevent tumorigenesis by inhibiting COX, but are also a risk factor for reflux and Barrett's disease. Increased expression of 5-LO pathway proteins is implicated in oesophageal adenocarcinoma, so we hypothesised that in vitro exposure of oesophageal tissue to an NSAID may induce transcriptional expression of genes for 5-LO pathway enzymes.

Methods Patients with known BO (n=14) were recruited as they attended endoscopy for routine surveillance. There was no evidence of dysplasia before or after this endoscopy. In each patient, oesophageal biopsies were taken from a single level of BO and from proximal squamous mucosa. Biopsies from each site were cultured for 15 h at 37°C in HEPES-buffered DMEM in the presence or absence of indomethacin (10 µM). Biopsies were then transferred to lysis buffer for quantification of mRNA for 5-LO, FLAP, LTA₄ hydrolase and LTC₄ synthase using quantitative RT-PCR. Transcript levels for each enzyme were calculated as mean ΔΔCt values compared to baseline expression after correction with a calibration sample across all plates.

Results Culture with indomethacin (10 µM, 15 h) significantly increased transcriptional expression of 5-LO (p<0.01) and FLAP (p<0.05) in squamous control biopsies, with a trend for increased LTC₄ synthase transcripts (p=0.08) but not LTA₄ hydrolase (p=0.38), suggesting induction of a cysteinyl-leukotriene biosynthetic pathway. Expression of the 5-LO pathway genes was elevated at baseline in Barrett's tissues and in vitro exposure to indomethacin did not produce further changes in this group (all p>0.2).

Conclusion These results indicate that indomethacin increases transcriptional expression of the proximal, rate-limiting enzymes of the 5-LO pathway in squamous oesophageal tissues, which may lead to increased enzyme activity and production of tumorigenic leukotrienes. This preliminary study suggests that brief NSAID exposure in vitro may mimic changes in the expression of 5-LO pathway genes induced in vivo in Barrett's metaplasia.

Competing interests None declared.

PTU-187 LONG-TERM QUALITY OF LIFE AFTER OESOPHAGECTOMY FOR CANCER: COMPARISON OF CERVICAL VS MEDIASTINAL ANASTOMOSES

doi:10.1136/gutjnl-2012-302514c.187

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Introduction With improvements in neoadjuvant therapy and earlier diagnosis, long-term survival after oesophagectomy for adenocarcinoma is becoming more frequent. With longer survival the quality of life (QOL) of patients post resection has become a greater priority. There has been extensive debate focusing on the long term effects of different sites for anastomosis. We aimed to examine if post-oesophagectomy QOL is affected by the site of the surgical anastomosis.

Methods QORTC C-30 and OG-25 QOL questionnaires were analysed from post-oesophagectomy patients surviving >3 years. Data were available both from a prospective database and questionnaires sent to post-oesophagectomy patients. Surgery was completed by two surgical teams and data were analysed in subsets dependant on the site of oesophago-gastric anastomosis—either thoracic or cervical. No patients underwent formal pyloroplasty. Data were analysed using the Student t test on SPSS statistical software. QORTC C-30 data were compared against the reference tables for oesophageal cancer pre-treatment and a cohort of pre-surgical patients awaiting oesophagectomy. Ethical approval was granted by the local MREC.

Results A total of 60 patients responded (82%, anastomosis: thoracic n=29, cervical n=31) with a median time post-surgery of 6.1 years (range 3–12 years). Cervical and thoracic anastomosis subgroups were equivalent in terms of age at time of surgery, time post op and cancer stage. No significant QOL difference was noted between cervical or chest anastomosis groups for any functional or symptom score, especially focusing on dysphagia (OG25, p=0.24), odynophagia (OG 25, p=0.68) and swallowing problems (OG25, p=0.73). The patients' overall general health (QL2) score was 72.0±19.43 (mean±SD) compared with 74.8±20.57 for a cohort of 53 NNUH pre-op oesophagectomy patients and 71.2±22.4 for the QORTC general population reference data. Functional indices and symptom scores are improved for our cohort compared to the QORTC oesophageal cancer reference baseline except symptom scores for diarrhoea and dyspnoea which worsen post-operatively.

Conclusion There is no significant difference in QOL scores between oesophagectomy patients with cervical or thoracic anastomosis at >3 years post-surgery when analysed using the QORTC C-30 and OG25 questionnaires. QOL in long-term survivors after oesophagectomy compares favourably with QORTC reference data for both pre-treatment oesophageal cancer and baseline general population data in our cohort, possibly due to the absence of pyloroplasty. Further prospective QOL data collection is required to elucidate any long-term differences between the two anastomosis sites.

Competing interests None declared.

PTU-188 "KNITTED" OESOPHAGEAL STENTS: SUPERIOR CONFORMABILITY WITH NO TRADE OFF

doi:10.1136/gutjnl-2012-302514c.188

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Introduction Knitted enteral stents have reduced stent shortening and no axial straightening forces, resulting in better conformability