Methods Here we screened a large cohort of GA patients for mutations in genes accounting for nearly 90% of reported mutations in GA in order to assess mutation frequencies. The screening was then followed by laser capture microdissection PCR sequencing and loss of heterozygosity (LOH) analysis of the mutated specimens in order to assess clonality of GA from dysplasia and IM.

Results From the 51 patients cohort we have found 18 patients (35.3%) presenting mutations, but only one out of the 51 patients (1.9%) presented two independent mutations in a single cancer. We found 3 mutations in APC (6.3%), one in CDKN2A (2.2%), 13 in TP53 (27.7%), one in CTNNB1 (2.2%) and one in K-RAS (2.4%), but none in PIK3CA or PTEN. Our mutation frequencies are comparable to previous reports, however we observed that most functional mutations occurred as a single event despite screening multiple genes. Analysis of the multiple laser capture microdissected areas revealed multiple genotypes within the same cancer in three out of the five patients. Moreover, current LOH data shows LOH of chromosome 17 in IM and throughout the cancers in all different genotypes, suggesting that chromosome 17 LOH might have been the first hit mutation followed by mutations in TP53, and in one patient a subsequent CTNNB1 mutation.

Conclusion This suggests that cancer progression may have been initiated by LOH in intestinal metaplasia and that GA cells might become genetically diverse as the cells evolve in the tumour. Therefore, IM is likely to represent a field defect for gastric cancer.

Competing interests None declared.

REFERENCES

1. **Gutiérrez-González L**, Graham TA, Rodríguez-Justo M, *et al*. The clonal origins of dysplasia from intestinal metaplasia in the human stomach. *Gastroenterology* 2011;**140**:1251–60.
2. **Thirlwell C**, *et al*. Clonality assessment and clonal ordering of individual neoplastic crypts shows polyclonality of colorectal adenomas. *Gastroenterology* 2010;**138**:1441–54.
3. **Leedham SJ**, *et al*. Individual crypt genetic heterogeneity and the origin of metaplastic glandular epithelium in human Barrett's oesophagus. *Gut* 2008;**57**:1041–8.

OC-101 PREDICTIVE FACTORS FOR POSTOPERATIVE MORTALITY AFTER RESECTION OF JUNCTIONAL AND GASTRIC ADENOCARCINOMAS

doi:10.1136/gutjnl-2012-302514a.101

W B Robb,* M Messenger, G Piessen, C Gronnier, N Briez, C Mariette. *Department of Digestive and Oncological Surgery, University Hospital Claude-Huriez, Lille, France*

Introduction Postoperative mortality (POM) within 30 days of oesophago-gastric resection remains significant and should be minimised to provide maximal chance of long-term survival. This study identifies factors predictive of 30-day POM in a large national multicentre cohort.

Methods A retrospective analysis was performed of 2670 patients (mean age 64±13 years) who underwent resection of junctional or gastric adenocarcinomas from 1997 to 2010 in 19 French centres. Ordinal data were compared using either the χ^2 test or Mann–Whitney U test, as appropriate. A stepwise logistic regression model was built to identify by multivariate analysis variables independently predictive of 30-day POM.

Results This study included 1893 men and 777 females, with a mean patient age of 64.2±13 years. 774 patients (29.0%) had a junctional, Siewert I or Siewert II type tumour and 1896 patients (71.0%) had either a Siewert type III or gastric adenocarcinoma. The majority of patients (2045, 76.6%) underwent gastrectomy, 625 (23.4%) oesophagectomy and proximal gastrectomy and 209 (7.8%) total oesophagogastric resection. Resection was R0 in 2224 patients (83.3%). Neoadjuvant treatment was given to 665 patients (24.5%).

A total of 114 patients died within 30 days of surgery (4.3%). POM rates increased during three study periods (1997–2000, 3.3%; 2001–2005, 3.6%; 2006–2010, 5.6%; $p=0.021$). The POM rate was significantly higher in patients who experienced grade III and IV toxicity during neoadjuvant chemotherapy when compared to those who did not (8.7% vs 2.6% respectively, $p=0.007$). Patients ≥ 60 years old and American Society of Anaesthesiology grade III or IV correlated with POM ($p=0.002$ and $p=0.000$, respectively). Variables indicating advanced disease consistently predicted POM (metastases at diagnosis, $p=0.005$; disease requiring extended resection, $p=0.005$; surgery with palliative intent, $p=0.042$) and no grade III or IV toxicity during neoadjuvant treatment (OR 0.286, 95% CI 0.107 to 0.762, $p=0.012$) were protective factors.

Conclusion This large national cohort study confirms patients with advanced disease are at higher risk of POM and centralisation of oesophago-gastric cancer resection is warranted. The novel finding that poor tolerance of neoadjuvant therapy increases the POM rate has significant implications for decision making in this subgroup of patients (Clinical Trial.gov identifier NCT01249859).

Competing interests None declared.

Pathology free papers

OC-102 COELIAC DISEASE, ANTI-INFLAMMATORY DRUGS OR HELICOBACTER PYLORI ARE THE MOST COMMON IDENTIFIABLE CAUSES OF LYMPHOCYTIC DUODENOSIS

doi:10.1136/gutjnl-2012-302514a.102

I Aziz,* K E Evans, A D Hopper, D M Smillie, D S Sanders. *Department of Gastroenterology, Royal Hallamshire Hospital, Sheffield, UK*

Introduction Lymphocytic duodenitis (LD) is found in 2% of duodenal biopsies. LD is defined by normal villous architecture and intraepithelial lymphocytes (IELs) >25 per 100 enterocytes. This is more commonly recognised as modified Marsh grade 1 on histopathology reports. Such patients should not be diagnosed with coeliac disease, solely by histology, as previous retrospective studies have suggested other associations with LD.

Aims To prospectively study the aetiology of LD.

Methods One hundred and sixty five patients with LD were rigorously investigated for coeliac disease and other known associations of LD, by means of revisiting the patient's history and recent investigations, followed by a combination of gluten challenge, HLA typing, repeat coeliac serology & duodenal biopsies, and exclusion of infection/inflammatory bowel disease.

Results 127 female: 38 male, age range 17–83 years, median age 46 years. Coeliac disease was present in 21% of patients with LD. In the absence of a positive coeliac diagnosis, LD was most commonly associated with anti-inflammatory drugs (17%), *H. pylori* (16%), gastrointestinal infections (7%), immune dysregulation (6%), inflammatory bowel disease (3%), and IgA deficiency (1%). Overall, there were 49 (30%) cases where no cause was found and the IEL count normalised in 35/49 (71%). Irritable bowel syndrome (IBS) was a clinical diagnosis in 30 of these 49 patients. All patients with coeliac disease were HLA DQ2 or DQ8 positive, compared to 55% of non-coeliacs (p value <0.0001). Patients with coeliac disease were significantly associated with positive endomysial and/or raised tissue transglutaminase antibodies ($p<0.0001$). There was no statistical difference in age, gender or baseline bloods (haematology/biochemistry/inflammatory markers) between the coeliac and non-coeliac group ($p>0.05$).

Conclusion This is the largest cohort of patients systematically investigated for a cause of their LD. A cause can be identified in up to 70% of cases, with coeliac disease, anti-inflammatory drugs and *H*

pylori representing the majority of cases. In those with no apparent cause, there may be an association with IBS and the IEL count becomes normal on repeat biopsy in 71%.

Competing interests None declared.

OC-103 TUMOUR REGRESSION GRADING CORRELATES TO SURVIVAL IN OESOPHAGO-GASTRIC CANCER. A REPORT OF CURRENT SURVIVAL OUTCOMES FOLLOWING NEO-ADJUVANT CHEMOTHERAPY

doi:10.1136/gutjnl-2012-302514a.103

¹A M Reece-Smith,* ²I Soomro, ³S madhusudan, ¹S L Parsons. ¹Department of Oesophago-gastric surgery, Nottingham University NHS trust, Nottingham, UK; ²Department of Histopathology, Nottingham University NHS trust, Nottingham, UK; ³Department of Medical Oncology, Nottingham University NHS trust, Nottingham, UK

Introduction Patients who demonstrate a histological response to chemotherapy as determined by tumour regression grading (TRG) are known to have improved survival.^{1 2} We report current survival expectations for patients following neo-adjuvant chemotherapy and resection of gastro-oesophageal cancer.

Methods TRG was determined by a specialist pathologist in 250 patients after chemotherapy, and survival outcomes were assessed by Kaplan–Meier analysis of patients divided into responder (Mandard TRG 1–3) and non-responder (TRG 4&5) groups, with log-rank comparisons.

Results After a median follow-up of 54.4 months survival was found to be improved in those with histological response to chemotherapy ($p<0.001$). Median survival was estimated to be 34.0 months and 21.2 months in oesophageal adenocarcinoma responders and non-responders and this was statistically significant ($p=0.050$). Junctional cancers demonstrated the largest survival difference at 51.1 months compared to 24.6 months ($p=0.003$). In gastric cancers the median survival was yet to be reached for responders and was 35.2 months for non-responders. However, smaller numbers in this group led to loss of statistical power ($p=0.166$). A higher proportion of patients with good response to chemotherapy was not seen using MAGIC regimen (Pearson χ^2 $p=0.616$). Good response to chemotherapy (TRG1–3) was associated with lower incidence of positive CRM ($p=0.021$).

Conclusion Tumour regression grading is a useful predictor of overall survival allowing clinicians greater ability to counsel their patients. However, MAGIC therapy appears to improve survival possibly through mechanisms other than simply increasing the proportion of patients that have histological response.

Abstract OC-103 Table 1 Proportion of patients achieving which tumour regression grades following either MAGIC regimen chemotherapy (three cycles of neo-adjuvant ECF/X) or other regimens (non-MAGIC)

TRG		1	2	3	4	5	Total
Non-magic	n=	3	5	24	33	35	100
	%	3.0%	5.0%	24.0%	33.0%	35.0%	100.0%
Magic	n=	8	12	31	46	41	138
	%	5.8%	8.7%	22.5%	33.3%	29.7%	100.0%
Total		11	17	55	79	76	238

Competing interests None declared.

REFERENCES

1. Becker, et al. *Ann Surg* 2011;**253**:934–9.
2. Fareed, et al. *Histopathology* 2009;**55**:399–406.

OC-104 THE VALIDITY OF THE ROYAL COLLEGE OF PATHOLOGISTS' STOMACH CANCER MINIMUM DATASET IN A POPULATION USING THE NORTHERN & YORKSHIRE CANCER REGISTRY DATA

doi:10.1136/gutjnl-2012-302514a.104

¹O Rotimi,* ¹H Grabsch, ²E Morris. ¹Department of Histopathology, Leeds Teaching Hospitals Trust, Leeds, UK; ²NYCRIS, Leeds Teaching Hospitals Trust, Leeds, UK

Introduction Quality histopathological reporting of resected stomach cancer provides important information for treatment of patients. Sub-standard reporting leads to incorrect staging which impacts on treatment and ultimately survival. Proforma reporting has been introduced as a means of standardisation. This study sought to validate the prognostic significance of the Royal College of Pathologists (RCPATH) stomach cancer dataset¹ in a population.

Methods A retrospective analysis of pathology forms from 1065 resected stomach cancer from 1995 to 2006 was carried out. The variables reported were related to NYCRIS registry survival data using univariate Kaplan–Meier method and Cox proportional regression modelling.

Results The study population was representative of the Yorkshire stomach cancer population. Survival was poorer with increasing age but it improved significantly from 29.0% (95% CI 23.1% to 35.1%) in 1995–1997 period to 50.5% (95% CI 40.1% to 60.1%) in the 2004–2006 period. Depth of local invasion, nodal stage and completeness of excision are validated as independent prognostic factors in a population setting. Importantly tumour differentiation is shown to be an independent prognostic factor. Patients recorded as well differentiated tumours had significantly better 3-year survival (61.3%; 95% CI 53.2% to 68.4%) compared to moderate (38.4%; 95% CI 33.2% to 43.6%) and poor differentiation (34.1%; 95% CI 30.1% to 38.1%)—Abstract OC-104 figure 1. The effect remains significant after adjusting for age and gender with HR of 1.74 (95% CI 1.11 to 2.71) for moderately differentiated and 2.1 (95% CI 1.3 to 3.4) for poorly differentiated tumours compared to well differentiated tumour.

Abstract OC-104 Figure 1 Kaplan–Meier survival estimates for differentiation ($p<0.0001$).

Conclusion The variables in the RCPATH stomach cancer dataset are validated to be of prognostic significance in a population setting. Importantly, the result showed that there is a significant survival differences between the three grades of differentiation. This is in contrast to the current recommendation by the RCPATH that well and moderately differentiated tumours be reported together as a single category.¹ We recommend separating this category in the next version of the RCPATH stomach cancer dataset guidelines.