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 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.

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

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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 oesophagogastrectomy. 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 8 resections/annum (OR 0.389, 95% CI 0.157 to 0.965, 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

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Introduction Lymphocytic duodenosis (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*