HOW OFTEN IS UPPER GASTROINTESTINAL CANCER MISSED DURING ENDOSCOPY?

Introduction Meta-analysis of published literature suggests that up to 14% of upper gastrointestinal cancer (UGIC) subjects have a negative oesophagogastroduodenoscopy (OGD) up to 3 years prior to diagnosis. We have examined how often UGIC is missed at OGD in our organisation and associated risk factors.

Methods Computerised OGD records from Sandwell General and City Hospitals between 1999 and 2007 were retrieved and submitted to the West Midlands Cancer Intelligence Unit (WMCIU) for UGIC registrations linkage. Subjects undergoing OGD 3 months to 5 years before diagnosis were identified as potentially missed UGIC cases and those with no OGD 3 months to 5 years before diagnosis served as controls. The influence of age, gender, indication, endoscopist specialty, trainee involvement, sedation use, number of biopsies taken, site and histology of UGIC on missed UGIC were examined by logistic regression analysis.

Results 36577 OGD records were submitted to WMCIU for cancer linkage and 524 UGIC were linked. 419 control UGIC: 388 (93%) negative OGD up to 3 years prior. 105 (20%) cases had OGD where abnormality at site of UGIC was seen but not potentially missed UGIC cases: 39 (37%) oesophageal cancer (OC) priassertly (within 90 days, with previous benign histology). 105 (20%) diagnosed at initial OGD; 31 (7%) diagnosed at repeat OGD approvally linked and 524 UGIC were linked. 419 control UGIC: 388 (93%) negative OGD up to 3 years prior. There is a high concordance between TPMT genotype and normal levels of 100% – 93% and low enzyme activity (93–100%); however the relationship is not biopsied or benign histology from an inadequate number of biopsies.<ref>±</ref> were associated with missed UGIC. The number of biopsies taken was significantly lower in the missed UGIC group than in the controls (2.1 ± 0.2 vs 5.4 ± 0.1, p < 0.05).

In subjects with OC, mid-oesophageal AC appeared more likely to be missed than lower-oesophageal AC (2.04, 0.99–4.23, p = 0.05). Oesophageal squamous cell carcinoma was much more likely to be missed than oesophageal adenocarcinoma (4.47, 1.88–10.65, p < 0.001). In GC subjects, there was no association between missed UGIC and tumour site (1.10, 0.61–1.97, p = 0.3) or histology subtype (1.09, 0.60–1.96, p = 0.9).

Age (1.5, 0.8–3.8, p = 0.2), endoscopist specialty (1.39, 0.70–2.76, p = 0.34), trainee involvement (1.2, 0.78–1.86, p = 0.59) and sedation use (0.98, 0.64–1.51, p = 0.9) were not associated with increased risk of missing UGIC.

Conclusion Missing UGIC at OGD was seen in 14.3% of subjects within 3 years of diagnosis. It was associated with lack of alarm symptoms, female gender, oesophageal squamous cell carcinoma and an insufficient number of biopsies from recognised abnormalities.

Disclosure of Interest None Declared

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CLINICAL AND ENDOSCOPIC IMPROVEMENT FOLLOWING HEMOPOIETIC STEM CELL TRANSPLANTATION VS MOBILISATION ALONE IN CROHN’S DISEASE

Introduction Pre-treatment measurement of red blood cell (RBC) thiopurine-S-methyltransferase (TPMT) activity is recommended to guide initial dosing of azathioprine (AZA) and mercaptopurine (MP). TPMT exhibits a trimodal distribution, with low and intermediate activities predicting myelotoxicity at standard drug doses. There is a high concordance between TPMT genotype and normal or low enzyme activity (93–100%); however the relationship is poor in the intermediate range (53–100%). Furthermore, there is a high concordance between TPMT genotype and normal or low enzyme activity (93–100%); however the relationship is poor in the intermediate range (53–100%).

Methods Patients with impaired quality of life due to active disease despite ≥3 immunosuppressive agents underwent mobilisation (iv cyclophosphamide 4 g/m² over 2 days then filgrastim 10 µg/kg/day) before randomisation to immediate (1 month) or delayed (15 months) HSCT. The conditioning regime was iv cyclophosphamide 50 mg/kg per day for 4 days, anti-thymocyte globulin 2.5 mg/kg/day and methyl prednisolone 1 mg/kg on days 3–5. The bone marrow was reconstituted by infusion of an unselected graft of 3–5 × 10^6/kg CD34+ve stem cells. Clinical (CDAI), endoscopic (SES-CD) quality of life and safety data are compared 1 year after mobilisation alone or after mobilisation and HSCT.

Results As of Jan 2013, data are available on 34/45 patients. Following mobilisation and HSCT, the CDAI fell from 317 (median, IQR 244–407) to 157 (71–246, n = 17) vs 351 (313–446) and 295 (220–370, n = 17) with mobilisation alone. The aggregate lower GI SES-CD score was 13.0 (8.5–24.5) before and 3.0 (1.5–10.0) after HSCT compared to 13.0 (6.5–15.5) before and 6.5 (3.5–17.8) after mobilisation alone. Over the whole study period 2012 there were 62 SAEs in 19 patients randomised to early transplantation (3.3 per patient) and 58 in 18 patients randomised to delayed transplantation (3.2 per patient). One patient died following HSCT. Final results of the study will be available to be presented for the first time at BSG 2013.

Conclusion Immunoablation and HSCT appears to be an effective treatment for CD that may substantially reduce endoscopic evidence of disease but incurs significant toxicity. The final results of the trial will allow a rational evaluation of the effectiveness and safety of HSCT to be discussed at BSG 2013.

Disclosure of Interest None Declared

THE INFLUENCE OF GENDER AND HAEMOGLOBIN ON TPMT ACTIVITY

Introduction The Autologous Stem Cell Transplantation Internation Crohn’s Disease (ASTIC) Trial is a randomised controlled trial co-sponsored by ECCC and EBMT and funded by the Broad Foundation that investigates immunoablation and hemopoietic stem cell transplantation (HSCT) in Crohn’s disease (CD) over 1 year: all patients will have reached this endpoint by April 2013.

Methods Patients with impaired quality of life due to active disease, despite ≥3 immunosuppressive agents all underwent mobilisation (iv cyclophosphamide 4 g/m² over 2 days then filgrastim 10 µg/kg/day) before randomisation to immediate (1 month) or delayed (15 months) HSCT. The conditioning regime was iv cyclophosphamide 50 mg/kg per day for 4 days, anti-thymocyte globulin 2.5 mg/kg/day and methyl prednisolone 1 mg/kg on days 3–5. The bone marrow was reconstituted by infusion of an unselected graft of 3–5 × 10^6/kg CD34+ve stem cells. Clinical (CDAI), endoscopic (SES-CD) quality of life and safety data are compared 1 year after mobilisation alone or after mobilisation and HSCT.

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are few explanations for the wide variation in inter-individual TPMT activities in the wild-type range. Bioavailability of the cofactor S-adenosylmethionine (SAM) and RBC age may play a role. The aim of this study was to determine if gender or anaemia influences RBC TPMT activity.

Methods We analysed a retrospective cohort of 6,496 RBC TPMT samples (n = 3804 females, n = 2692 males) measured in the PRL since 2004 and correlated enzyme activity with gender and haemoglobin concentrations.

Results A greater portion of females exhibited intermediate TPMT activity (13.46%) as compared to males (11.07%). The mean TPMT activity was also significantly lower in females with an Hb $< 12$g/dl (n = 250, mean TPMT 32.46 pmol/mg Hb/h) versus males with an Hb $> 12$g/dl (n = 2192, mean TPMT 32.94 pmol/mg Hb/h; p = < 0.0001). Similarly TPMT activity was significantly higher in male patients with an Hb $< 10$g/dl (n = 123, mean TPMT 32.46 pmol/mg Hb/h; p = < 0.0001). The finding of higher TPMT activity in anaemia may be due to a younger red cell population in this group. The difference in TPMT activities between patients with or without anaemia is clinically relevant, particularly where the TPMT activity is significantly higher in female patients with an Hb $< 10$g/dl (n = 125, mean TPMT 32.14 pmol/mg Hb/h; p = < 0.0001) versus males with an Hb $> 12$g/dl (n = 1901, mean TPMT 35.76; p = < 0.0001).

Conclusion TPMT activity in the wild-type range is lower in females than males, suggesting a post-translational influence on TPMT activity related to gender. Lower levels of SAM have been reported in females, which may explain this observation. Re-appraisal of the concordance between TPMT genotype and phenotype, adjusting for gender is therefore indicated. The finding of higher TPMT activity with anaemia may be due to a younger cell population in this group. The difference in TPMT activities between patients with or without anaemia is clinically relevant, particularly where the TPMT activity is significantly higher in female patients with an Hb $< 10$g/dl (n = 125, mean TPMT 32.14 pmol/mg Hb/h; p = < 0.0001) versus males with an Hb $> 12$g/dl (n = 1901, mean TPMT 35.76; p = < 0.0001).

Disclosure of Interest None Declared

REFERENCES

OC-016 ELEVATED FACIAL CALPROTECTIN PREDICTS DISEASE PROGRESSION IN CROHN'S DISEASE
doi:10.1136/gutjnl-2013-304907.018

Abstract OC-016

Introduction Historical cohort studies have clearly demonstrated that over time the majority of patients with Crohn’s disease (CD) will progress from inflammatory (B1) to strictureing (B2) or fistulizing (B3) disease. Emerging data suggest that more intensive treatment targeted towards mucosal healing will help to prevent disease progression. Faecal calprotectin (FC) is an established surrogate biomarker for endoscopic mucosal healing. It has yet to be established whether tailoring therapy to FC levels prevents disease progression.

In the present study we aimed to determine whether FC levels in patients with established CD were predictive of disease progression.

Methods The Edinburgh Faecal Calprotectin Registry (EFCR) comprises data on 22,130 FC assays in 16,278 patients from 2005–2012. Detailed phenotypic information was obtained on patients with CD by retrospective casenote review. Data collected included demographics, disease location, disease behaviour over time, CD-related surgery, investigations, hospitalisations and drug therapy.

Patients were included in the main analysis if they had at least 12 months’ follow-up since first FC. The a priori primary endpoint was a composite of progression in Montreal luminal behaviour, hospitalisation for flare and resectional surgery.

Results There were 881 CD patients identified with at least one FC, of which 723 had at least one year’s follow-up, with median follow-up time 40 months (IQR 25–60). The median age was 28y (IQR 20–42) at diagnosis and 40y (28–53) at time of first FC.

239 patients (33%) reached the primary endpoint, of whom 68 had had progression of their Montreal behaviour from B1 to B2 or B3, or from B2 to B3.

The median of the earliest FC was significantly higher in the group that reached the primary endpoint at 586 µg/g (IQR 210–1235) vs. 289 (75–1001) in those that did not (p < 0.0001). Survival analysis (Fig 1) revealed significant differences in time to progression, hospitalisation or surgery with calprotectin $\geq 200$ (p < 0.0001).

Conclusion This large single-centre study presents compelling evidence that measurement of FC can be used to predict disease course, which creates the opportunity for physicians to intervene earlier and perhaps alter the disease course.

Disclosure of Interest None Declared

OC-017 A DISCRIMINANT ANALYSIS DEMONSTRATES THAT SIBLINGS OF PATIENTS WITH CROHN'S DISEASE HAVE A DISTINCT MICROBIOLOGICAL AND IMMUNE PHENOTYPE COMPARED WITH HEALTHY CONTROLS: INSIGHTS INTO DISEASE PATHOGENESIS
doi:10.1136/gutjnl-2013-304907.017

Introduction Crohn’s disease (CD) is associated with genetic risk, intestinal dysbiosis, altered blood T-cell phenotype, increased faecal calprotectin (FC) and intestinal permeability (IP). Factors shared by CD patients and unaffected siblings may be implicated in CD pathogenesis.