Conclusion Radiation exposure in Crohn's disease appears to be increasing despite new modalities such as ultrasound and MRI. The increase is attributed to the increased use of CT scanning, as availability and accuracy of imaging via CT in Crohn's disease have improved in recent years. With the gradual introduction of low-dose CT scanning, we would hope these levels will fall again in the near future. Furthermore we observed an increase in the use of plain abdominal films of 87.5%. We feel this may be attributable to the shift in attitude towards treating unwell patients with the increasingly effective and available pharmacological therapies, rather than surgical options, although further audit should be carried out to establish if this is indeed the case.
Disclosure of Interest None Declared

Neoplasia and cancer pathogenesis free papers

OC-066 THE CANCER RESEARCH UK (CRUK) FUNDED ICGC OESOPHAGEAL ADENOCARCINOMA PROJECT: MRC RESEARCH CENTRE AND CRUK CAMBRIDGE RESEARCH INSTITUTE

doi:10.1136/gutjnl-2013-304907.065

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Introduction Esophageal adenocarcinoma (EAC) has one of the fastest rising incidences of any cancer in the western world. With a 5-year survival below 10% it is one of the most common causes of cancer death in US and UK. Currently little is understood about the genetic alterations that drive the development of OAC. Better understanding of these alterations may allow the development of novel therepeutic approaches
Methods We have performed whole genome sequencing on 22 cases. Targeted amplicon resequencing of 27 recurrently mutated genes was performed on a validation cohort of 100 further oesophageal adenocarcinomas.
Results In the discover set of 22 OACs we identified recurrent mutations (>3 tumours) in 31 genes including several implicated in tumorigenesis; TP53, CDKN2A, ARID1A. Strikingly in the validation cohort we observed that > 30% of EAC samples harbour mutation of one or both of the SWI/SNF complex members ARID1A and SMARCA4. In addition we identified highly recurrent mutations in several additional genes including TRIM58, SSTR4 and MYO18B.
Conclusion Whole genome sequencing provides an unbiased screen of mutational architecture of OAC. This has allowed the identification of several recurrently mutated genes not previously implicated in this disease providing a unique insight to it's pathogenesis
Disclosure of Interest None Declared

OC-067 AN EXPRESSION SIGNATURE OF THE ANGIOGENIC RESPONSE IN GASTROINTESTINAL NEUROENDOCRINE TUMOURS: CORRELATION WITH TUMOUR PHENOTYPE AND SURVIVAL OUTCOMES

doi:10.1136/gutjnl-2013-304907.066

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Introduction Gastroenteropancreatic neuroendocrine tumours (GEPNETs) are heterogeneous with respect to biologic behaviour and prognosis. Since angiogenesis is a renowned pathogenic hallmark as well as a therapeutic target, we aimed to investigate the prognostic and clinico-pathological role of tissue markers of hypoxia and angiogenesis in GEPNETs.
Methods Tissue microarray (TMA) blocks were constructed with 86 tumours diagnosed from 1988 to 2010. TMA sections were immunostained for Hypoxia inducible factor 1α (Hif-1α), Vascular Endothelial Growth Factor A (VEGF-A), Carbonic Anhydrase IX (CaIX) and Somatostatin receptors (SSTR) 1 to 3 and Ki-67. Biomarker expression was correlated with clinico-pathological variables and tested for survival prediction using Kaplan-Meier and Cox regression methods.
Results Eighty-six consecutive cases were included: 51% male, median age 51 (range 16–82), 68% presenting with a pancreatic primary, 95% well differentiated. Forty-four cases (51%) had distant metastases (liver 72%, lymph nodes 28%). Median tumour size was 3.0 cm (range 0.6–12.5). Vascular invasion and necrosis were present in 20 (23%) and 18 (21%) of the specimens. Median overall survival (OS) was 8.8 years (range 0.1–13.5). Overexpression of CaIX was observed in 10% of the specimens, VEGF-A in 78%, Hif-1α in 59%, SSTR1 in 17%, SSTR2 in 31% and SSTR3 in 1%. Ki-67 index was obtained in all cases and scored as G1 in 84%, G2 in 13% and G3 in 4%. SSTR2 overexpression was predominant in pancreatic NETs ($p < 0.01$), whilst Hif-1α was predominant in non pancreatic NETs ($p = 0.05$). Higher Ki-67 labelling was associated with larger tumour size ($p < 0.001$) and necrosis ($p = 0.03$). Overexpression of Hif-1α and VEGF-A correlated with the presence of liver metastases ($p < 0.001$). Patients with Ki-67 count > 1% ($p = 0.02$), high Hif-1α and low SSTR2 expression ($p = 0.03$) displayed significantly shorter OS times.
Conclusion We have identified a coherent expression signature by immunohistochemistry that can be used for patient stratification and to optimise treatment decisions in GEPNETs. Tumours with low proliferation index, preserved SSTR2 and low Hif-1α expression have an indolent phenotype and may be offered less aggressive management and less stringent follow up.
Disclosure of Interest None Declared

OC-068 ALGORITHMIC MANAGEMENT OF RADIATION-INDUCED GI SYMPTOMS IS HIGHLY EFFECTIVE: THE ORBIT RANDOMISED CONTROLLED TRIAL

doi:10.1136/gutjnl-2013-304907.067

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Introduction Chronic gastrointestinal (GI) symptoms after pelvic radiotherapy are common. Most affected patients never see a GI specialist. We developed a comprehensive algorithm to direct management of new GI symptoms after pelvic radiotherapy. A 3 arm randomised controlled trial was performed to test 2 hypotheses: (1) Algorithm directed intervention is beneficial compared to no intervention (2) outcomes are not worse when patients are managed by a nurse rather than a gastroenterologist.
Methods Patients treated with pelvic radiotherapy > 6 months earlier with persisting GI symptoms were randomised to management according to the algorithm by 1. a GI nurse or 2. gastroenterologist or 3. the self help Macmillan booklet "Pelvic Radiotherapy: Possible Late Effects". After 6 months, booklet arm patients with persisting symptoms could ask to see the gastroenterologist. Patients in the nurse arm were transferred to the gastroenterologist if they had problems beyond the algorithm's scope. The primary end point was change in the modified Inflammatory Bowel Disease Questionnaire – bowel sub score (IBDQ-B) at 6 months. Follow up continued until 12 months. The trial had 80% power to answer the 1st hypothesis after randomising 196 patients and the 2ndafter closing the booklet arm, and randomising 22 more patients to gastroenterologist or nurse.