O67 IMPROVED OUTCOMES OF OESOPHAGO-GASTRIC CANCER TREATMENT OVER 15 YEARS
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Introduction: Treatment of potentially curative oesophago-gastric carcinoma has evolved over the last 15 years, but remains challenging. Improvements in early detection and stage, surgical and peri-operative care in conjunction with oncological therapy are hypothesised to have improved survival.

Method: A retrospective analysis was undertaken on patients that had undergone oesophago-gastric cancer resection between 2001-2016 at a single centre. Three 5 year patient cohorts were defined (2001-05, 2006-10, 2011-16) and examined to understand changes in presentation, stage, surgical and oncological intervention and survival over this time period.

Result: The 1617 patients were divided by operative date into equivalent sized cohorts (n= 517, 561, 539). The median age (69 years) remained similar over time, but with a small increase in co-morbidity (median charlson index = 5). Leak (5-9%) and overall complication rates (24-30%) were comparable. The proportion of patients with locally advanced disease (stage III) progressively increased over the 15 years (42%, 47%, 49%), whilst the R1 resection rate progressively fell from 36 to 28%. Administration of oncological therapy (neo-adjuvant, peri-operative and chemo-radiotherapy) rates increased (24%, 53%, 68%) over time. Over the three different 5-year time periods, 30 day mortality progressively fell (6%, 5%, 3%) and median overall survival significantly improved (23, 26, 36 months). This survival data represents considerably older and comorbid patient group, with markedly greater proportion of advanced stage disease than other published series.

Conclusion: Advances in peri-operative, surgical and oncological therapy have improved overall survival in the last 15 years, despite an increase in advanced disease stage.

Take-home message: Advances in peri-operative, surgical and oncological therapy have improved overall survival from oesophago-gastric carcinoma over the last 15 years.

O68 BARIATRIC SURGERY ASSOCIATED WITH REDUCED MORTALITY IN THE MORBIDLY OBESE: A CLINICAL PRACTICE RESEARCH DATALINK STUDY
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Introduction: Patients who are morbidly obese (BMI≥35kg/m2) are at increased risk of all-cause mortality as a result of metabolic sequelae including: hyperlipidaemia, hypertension and diabetes. Bariatric surgery has been shown to reduce the severity of the metabolic complications of obesity. This study aimed to analyse the clinical practice research datalink (CPRD) to identify which factors are prognostic of all-cause mortality in the morbidly obese.

Method: A case-controlled analysis was carried out of patients with a BMI≥35kg/m2 from the CPRD. Clinicopathological characteristics at baseline diagnosis were extracted. Cases of all-cause mortality were identified as a clinical endpoint. A cox proportional hazard model was used to calculate hazard ratios (HRs) for different patient factors. A p-value<0.050 was defined as significant.

Result: 187,061 were identified for analysis. Median follow-up time was 98.0 months (range:0.0-1095.0 months). 8,655 (4.6%) were identified as having died over the study period. The median time from baseline obesity diagnosis until death was 137.0 (range: 3.0-628.7 months). Multivariate analysis found bariatric surgery to be associated with reduced risk of all-cause mortality (HR:0.502;p<0.001). The following were associated with increased risk of death: males (HR:1.777;p<0.001), BMI≥60 (HR:2.477;p<0.001); Charlson score>3 (HR:1.833;p<0.001); hypertension (HR:2.080;p<0.001), diabetes (HR:2.142;p<0.001) and hyperlipidaemia (HR:1.743;p<0.001).

Conclusion: Bariatric surgery was shown to be associated with reduced risk of all-cause mortality. Factors such as high BMI diabetes, hyperlipidaemia and hypertension at first diagnosis of morbid obesity were each independently associated with an increased risk of death. By reducing the prevalence and severity of the sequelae of obesity, bariatric surgery can prolong patient survival.

Take-home message: Bariatric surgery is associated with a reduction of all-cause mortality in a morbidly obese population.

O69 THE PANCREATIC EPSILON-CELLS RECOVER THE EMBRYONIC GHERELIN SECRETION IN RESPONSE TO BARIATRIC SURGERY
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Introduction: Many surgical techniques are employed in the treatment of obesity. A main consequence of these techniques is the severe improvement of Type 2 Diabetes mellitus. Many hypotheses had been exposed to know the intrinsic mechanism developed in this relationship. The enterohormones seems to be a definitive effector. The ghrelin is an enterohorm that have the capacity to release ghrelin during the embryonic stages. We studied the changes in the ghrelin immunostaining in endocrine pancreas of rats which underwent bariatric surgery. MATERIAL AND

Method: We employed 16 non obese euglycemic male Wistar rats, randomised in the surgical groups. These groups were the surgical techniques (Sleeve gastric –SG- and Roux en Y Gastric Bypass –RYGB-),
and two controls (fasting and surgical). After three months, rats were sacrificed; the pancreas were obtained and processed for the immuno-cytochemical technique.

**Result:** We reported a significant increase of epsilon cells (ghrelin positive/mm2 pancreatic area) in the pancreas of SG versus the control groups (vs FC, P<0.01 and vs sham, P<0.05). CONCLUSION. SG and RYGB are surgical techniques broadly employed in humans and both reduce severely the fundus. Paradoxically, the serum level of ghrelin in patients are preserved. We reported that the total suppression of the fundus gastric produced the recovery of an embryonic pancreatic function. This mechanism could be related with the complex physiologic mechanism that improve T2DM after bariatric surgery.

**Take-home message:** The hormone ghrelin recover a releasing embryonic function in the pancreas after bariatric surgery.

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**O70  EXPLORING THE MULTICELLULAR ECO-SYSTEM OF OESOPHAGEAL CANCER**

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**Introduction:** Genomic profiling of oesophageal adenocarcinoma (OAC) fails to reliably distinguish between tumour phenotypes. Bulk sequencing dictates selection bias at the expense of tumours with abundant stroma; shown to be associated with the worst prognoses. Understanding transcriptional variation between individual cells is an important way of learning about complex tissues and functional responses.

**Method:** Highly-parallel genome-wide expression profiling of single cells using nanoliter droplets (DropSeq) was applied to primary tumour and matched normal tissue from oesophageal resections. Fragmented cDNA (~1,000 cells/sample) was amplified and sequenced on Illumina NextSeq-500. SEURAT (v2.0, R-package) was used to identify highly-variable genes and perform clustering to discover differentially-expressed genes between cell populations.

**Result:** 5877 high quality cells were recovered from 5 tumours expressing 21657 genes. Unsupervised clustering using 4391 most variable genes revealed 25 different cell populations including 9 distinct tumour, 4 fibroblast and 6 immune populations. A sub-population of 90 cells from the most advanced cancer (T3N3) were differentiated from other cancer cells by expression of genes from the BRCA1-PI3K network, upregulated in invasive breast cancer cells, and genes co-expressed in multiple stem-cell populations. Gene-ontology showed cancer fibroblasts transcribed factors involved in cell motility, angiogenesis and immune modulation.

**Conclusion:** Interrogating OAC at the single cell level demonstrates a complex cancer ecosystem of malignant and non-malignant cells. This powerful adaptation of novel technology allows us to identify active cellular pathways that cannot be identified in bulk-sequencing studies, are unique to malignant tissue and could be targeted for disruption by novel therapies.

**Take-home message:** We have adapted a novel technology to interrogate thousands of cells at a time from multiple tumours. We can use this technology to identify pathways and cell-cell interactions that influence the behaviour and phenotype of cancers and could be targeted in future therapies.

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**O71  POSTOPERATIVE COMPLICATIONS IMPACT LONG-TERM SURVIVAL, BUT NOT DISEASE RECURRENCE, FOLLOWING OESOPHAGO-GASTRIC CANCER RESECTION**

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**Introduction:** Postoperative complications following the resection of oesophago-gastric carcinoma can result in considerable early morbidity and mortality, however the long-term effects are less clear. Reports in international literature are mixed, so it remains unclear if leak and other complications reduce overall survival and disease free survival, as has been demonstrated in colorectal cancer.

**Method:** A retrospective analysis was undertaken on a prospectively compiled database of 1100 patients that underwent oesophageo-gastric cancer resection between 2006-16 at a single UK centre. Patients were stratified by complication (defined by Clavien-Dindo (CD)), to determine the effect of leak and non-leak related complications on overall survival, cancer recurrence and disease free survival.

**Result:** The median age was 69 years, charleson co-morbidity index was 5, and 48% had stage III disease, with cancer recurrence in 39%. Post-operative complications occurred in 29%; ward based complications (CD II) occurred in 13.8%, leak related complications (CD III-IV) in 7.3% and severe non-leak related complications (CD III-IV) in 7.8%. Patients stratified as: No complications, leaks and non-leak complications had a median overall survival of 36, 40 and 19 months, and a disease free survival of 32, 18, and 35 respectively. The reduction in overall survival, but not disease free survival, following severe non-leak related complications was significant (log rank <0.05).

**Conclusion:** This contemporary UK cohort is the second largest internationally. It supports US and Japanese findings that whilst leak does not affect survival, other severe postoperative complications do significantly reduce overall survival, but not disease recurrence.

**Take-home message:** Postoperative complications impact long-term survival, but not disease recurrence, following oesophageo-gastric cancer resection.
THE RISK OF VENOUS THROMBOEMBOLISM AFTER SURGERY FOR OESOPHAGO-GASTRIC MALIGNANCY AND THE IMPACT OF CHEMOTHERAPY: A POPULATION BASED COHORT STUDY

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Introduction: This study investigated incidence of venous thromboembolism and effects of chemotherapy in a population of patients undergoing surgery for oesophageal or gastric cancer.

Method: We used linked primary (Clinical Practice Research Datalink) and secondary (Hospital Episode Statistics) care data. The Office of Population, Censuses and Surveys (OPCS) Classification of Surgical Operations and Procedures version 4 codes were used to identify patients by type of surgery and chemotherapy. Crude rates and adjusted hazard ratios (HRs) were calculated for rate of first VTE following oesophagectomy or gastrectomy using a Cox regression model.

Result: We identified 2452 patients, with 1012 patients undergoing gastrectomy and 1440 oesophagectomy. Median age was 67 years (interquartile range (IQR) 59-74). The rate of VTE was highest in the first month with absolute VTE rates of 114 per 1000 person-years (95% CI 59.32-219.1) and 172.73 per 1000 person-years (95% CI 111.44-267.74) in gastrectomy and oesophagectomy respectively. In the gastrectomy group neoadjuvant and adjuvant therapy was associated with a six-fold increased risk of VTE, HR 6.19 (95% CI 2.49-15.38). However in the oesophagectomy group no association was observed, HR 1.7 (95% CI 0.7-3.92).

Conclusion: Patients undergoing surgery for oesophageal and gastric cancer are at an increased risk of VTE if they have had chemotherapy (neoadjuvant, adjuvant or both) compared to no chemotherapy. This could reflect risks attributable to the underlying disease, surgical procedure, chemotherapy treatment or, more likely, a combination of these and other factors.

Take-home message: Patients undergoing surgery for oesophago-gastric cancer are at an increased risk of VTE, particularly in the setting of chemotherapy.

A SYSTEMATIC REVIEW OF VENOUS THROMBOEMBOLISM RATES AFTER SURGERY FOR OESOPHAGEAL OR GASTRIC CANCER

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Introduction: In oesophago-gastric cancer there is marked variation in the quoted incidence of venous thromboembolism (VTE). This study aimed to summarise existing literature and determine incidence of VTE after surgical resection; or surgery with chemotherapy for oesophageal or gastric cancer.

Method: A comprehensive search of Embase and Medline databases from 1974-2017 was undertaken to identify population based studies, where patients had a diagnosis of oesophageal or gastric cancer. Data was extracted for the number of participants with clinically significant VTE. Total person-years of follow up and 30-day incidence rates of VTE for each study were calculated if not stated. Incidence rates of VTE were pooled using the generic inverse variance method.

Result: 15 studies met inclusion criteria reporting on 139,212 patients. The pooled incidence rate of VTE following oesophageal resection only was 347 per 1000 person years (95% CI 316-381). The pooled incidence rate of VTE in those treated with oesophageal resection and chemotherapy was 643 per 1000 person years (95% CI 542-763). The pooled incidence rate of VTE for gastric resection was 82 per 1000 person years (95% CI 76-89) and that for gastric resection with chemotherapy was 180 per 1000 person years (95% CI 76-89).

Conclusion: The incidence of VTE events following oesophago-gastric surgery is high. The rates are further increased in the setting of chemotherapy, reinforcing the need for extended thromboprophylaxis in this category of patients. However statistical heterogeneity in the available literature highlights the need for more methodologically robust population based studies in this field.

Take-home message: VTE rates after oesophagogastric cancer surgery is high and is further increased in the setting of chemotherapy. There may be a need for extended VTE prophylaxis beyond the current regimen.

CUMULATIVE SUM (CUSUM) ANALYSIS OF POST-OPERATIVE PNEUMONIA, BUT NOT MORTALITY OR ANASTOMOTIC LEAK, IS A USEFUL TOOL FOR REAL-TIME OUTCOME MONITORING

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Introduction: Prospective, risk-adjusted outcome monitoring using cumulative sum charts (CUSUM) is routine practice in cardiac surgery and burns intensive care and is potentially of use in oesophago-gastric surgery.

Method: Seventy-two oesophagogastric cancer resections from a single high volume cancer centre over a 12-month period were entered to a retrospective CUSUM tool. Individual risk of 30 and 90-day mortality, anastomotic leak, and pneumonia were calculated as per methods previously published.
CUSUM charts and variable life-adjusted displays (VLADs) of outcomes (30- and 90-day mortality, anastomotic leak, pneumonia) were plotted.

**Result:** There were no post-operative deaths and four anastomotic leaks during the study period. There were 31 cases (43%) of post-operative pneumonia requiring antibiotic treatment. CUSUM and VLAD charts demonstrated this to be primarily focussed late in the series, with the VLAD trace deviating from the expected rate between cases 63 and 70 (correlating with a reduction in physiotherapy provision). CUSUM monitoring of pneumonia, but not mortality or anastomotic leak, appears to be a useful dynamic representation of patient outcomes after OG resection.

**Conclusion:** CUSUM could improve routine monitoring of outcomes after major oesophago-gastric surgery. The ability to identify negative trends in outcomes in real-time may allow a unit to identify key factors and audit their practice. Identification of periods of above expected outcome could be used as opportunities to reflect upon and reinforce positive factors, enthuse the wider surgical team and give confidence to patients. Post-operative pneumonia may be a better indicator than mortality or anastomotic leak due to its higher incidence.

**Take-home message:** Cumulative sum charts, which are used routinely in cardiac surgery and burns intensive care, could be used to improve outcomes of patients in other specialties, including oesophago-gastric surgery.