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Giant hiatus hernia (GHH) is usually symptomatic and can have significant impact on a patient's quality of life. There is ongoing debate about optimal technique of giant hiatus hernia repair. This paper aims to look at the outcomes of laparoscopic composite repair of giant hiatus hernia from a large single centre cohort.

Methods: A retrospective analysis of prospectively maintained database was performed. Patients undergoing composite repair for GHH defined as >30% stomach above diaphragm were included. Primary outcome was hernia recurrence. Secondary outcomes were perioperative morbidity and mortality, correlation of symptoms and hernia recurrence post operatively, need for revision surgery, resolution of symptoms post operatively and patient self-reported quality of life (GIQOL, Visik score).

Results: Inclusion criteria were met by 221 patients. Post-operative endoscopic and/or barium swallow follow up was performed in 198 patients with 23.74% recurrence rate. There was no correlation with recurrence of hernia and persistent post-operative symptoms.

The most common presenting symptom was shortness of breath, followed by dysphagia, chest pain and heartburn. Dysphagia was most common post-operative symptom.

There was significant improvement in QOL post-operatively.

Conclusion: Laparoscopic composite repair was proven safe and effective in this cohort. Hernia recurrence was not associated with ongoing symptoms and did not have an effect on QOL. A small proportion of patients with recurrence required revision surgery. Overall satisfaction with surgery was high.

471 POTENTIAL ROLE OF NEOADJUVANT RADIO-CHEMOTHERAPY ON NEW-ONSET ATRIAL FIBRILLATION AFTER HYBRID IVOR-LEWIS ESOPHAGECTOMY FOR CANCER

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New onset atrial fibrillation (AF) is observed in up to 37% of patients after esophagectomy for esophageal and esophago-gastric junction (EGJ) cancer. Little is known about risk factors for AF in this cohort of patients. Current literature describes an association between postoperative AF and other complications, notably anastomotic leaks and infective or pulmonary complications. The aim of this paper is to determine which factors relate to an increased risk of new-onset AF after esophagectomy.

Methods: We retrospectively analyzed a prospectively collected database in a high-volume, tertiary referral center for esophageal disease. All consecutive patients who underwent hybrid Ivor-Lewis (IL) esophagectomy for esophageal or EGJ cancer at the Upper GI surgery unit in Humanitas Research Hospital from January 2018 to august 2019 were evaluated for inclusion. Patients with a history of paroxysmal or chronic AF were excluded from the analysis. Complications were reported according to the ECCG classification. Association between variables and onset of AF was studied with univariable and multivariable logistic regression analysis.

Results: 89 IL cases among 125 esophagectomies were included for analysis. Overall complication rate was 29.2%. AF accounted for 9 cases (10.1%) and was the only complication in these patients. Anastomotic leak occurred in 2 patients (2.25%) both ECCG type 1, 3 developed significant pleural effusion (3.37%), 6 other infective conditions (6.7%). No postoperative deaths occurred. Significantly increased risk of AF was found in patients who underwent chemoradiotherapy(CRT) compared to those who received chemotherapy(CT) or no treatment(OR = 8.4, p = 0.02). If we compare only patients who received neoadjuvant treatment, a higher risk for CRT versus CT alone was found(OR = 5.5), with a trending significance(p = 0.08).

Conclusion: In this study, we did not find any association between AF and other complications. New-onset AF always presented as the only complication and it was significantly associated to neoadjuvant chemoradiotherapy. On the basis of this findings, we are designing a protocol with the aim of studying potential preventive intervention for postoperative FA after esophagectomy.

474 GENOMIC ANALYSIS OF RESPONSE TO NEOADJUVANT CHEMOTHERAPY IN ESOPHAGEAL ADENOCARCINOMA

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In the UK, neoadjuvant chemotherapy (NAC) for locally advanced esophageal adenocarcinoma (EAC) is the standard of care. Unfortunately, response to NAC, following surgery is often low (<30%) and survival benefit at 2 years is only 5.1%. The EAC genome is complex and heterogeneous between patients, where specific mutagenic processes and mutations may result in chemotherapy resistance. Here we report preliminary results from whole-genome sequencing (WGS) of 48 patients who were subsequently treated with NAC.

Methods: We defined response as Mandard Tumor Regression Grade (TRG) 1-2 (n = 15) and non-response as TRG4-5 (n = 33). WGS of 50x coverage and calling of genomic events (Strelka2, SCAT/GISTIC) was performed according to Frankell Nat Genet 2019 with modifications, to differentiate driver from passenger mutations (dNdScv, oncodriveCLUST), determine variant allele frequencies (VAF; copy number-adjusted) and mutation signatures (NMF R-package). Following stringent variant QC (Phred score ≥ 30), filtering (VAF >0.02) and annotation (ANNOVAR, cancer census/helper, the 77 known EAC drivers and false positive genes) and visualisation in maftools, we evaluated the data for associations between genomic events and response to NAC.

Results: COSMIC mutation signatures 2 (TRG1-2; Cosθ = 0.89) and 6 (TRG4-5; Cosθ = 0.82) were enriched, suggesting defective mismatch repair in non-responders. Using 5,193 high-confidence non-silent mutations (TRG1-2,n = 1969; TRG4-5, n = 3224), we identified 39 mutated driver genes (Figure-1) with a median of 2.9(0-5) (TRG1-2) and 2.7(0-9) (TRG4-5) driver events/patient. Shared dysregulated pathways, included DNA-damage (TP53), cell cycle (CDKN2A), TGF-β (SMAD4) and chromatin regulation (ARID1A). There was no difference in the prognostic of SMAD4 and GATA4 genes. Interestingly, NAV3 mutations were only present in non-responders (21%,7/33); and in responders TP53 incidence was higher (93% vs. 58%) with a concomitant reduction in clonal cell fraction (0.25 vs. 0.39;Wilcoxon, p < 0.0001).

Conclusion: The data suggest that specific genomic events, such as NAV3 mutation and the intra-tumoral heterogeneity of mutated DNA-damage response genes may offer additional predictive value. Ongoing work includes analysis of the impact of non-coding variation on response. While our analysis is limited by sample size and requires validation in additional cohorts, it demonstrates the potential of genomic sequencing to identify NAC response biomarkers and may guide alternative or novel treatment modalities for chemo-resistant tumours.

481 EXPRESSION OF ANDROGEN RECEPTOR AND HER 2/NEU IN ESOPHAGEAL SQUAMOUS CELL CARCINOMA AND ITS MICOENVIRONMENT

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Esophageal cancer (EC) is the sixth most common cause of cancer-related deaths. Esophageal squamous cell carcinomas (ESCCs) have a higher incidence and worse prognosis in males, which may be dependent on the difference of environment of sex steroids. The influence of androgen receptor (AR) and HER 2/neu expression on hormone-related cancers are well known but their role in EC shows conflicting data. This warrants further investigation on their influence on tumor microenvironment of EC.

Methods: All the cases of biopsy proven primary ESCC which presented to the institute in the years 2016–2020 were included. Patients undergoing neoadjuvant therapy were excluded.

Epidemiological and pathological data were noted from the patient records. Paraffin embedded tissue samples of the patient were collected and immunohistochemical staining (IHC) for AR and HER 2/Neu was performed. The stained slides were then scored independently by three pathologists.