Methods: The effects of immune checkpoint blockers were characterised in terms of proliferation, cytolysis and cancer cell viability. The basal expression of immune checkpoints (TIGIT, PD-1, PD-L1, PD-L2) and Damage Associated Molecular Patterns (Calreticulin, HMGB1) in EAC patients was profiled ex vivo using fresh tumor, blood and lymph-node tissue (n = 10) by flow cytometry. In an in-vitro study, T-lymphocytes were isolated and treated with Nivolumab, Pembrolizumab or Atezolizumab, activated and co-cultured for 48 hours with a panel of four esophageal cancer cell lines; OE33P, OE33R, FLO-1, FLO-1LM treated with 1.8Gy and 3.6Gy of radiation (Fig 1). Cytolysis was measured using a CCK8 assay.(n = 6).

Results: The expression of TIGIT, TIM-3, PD-1 and its ligands (PD-L1, PD-L2) were higher ($p < 0.001$) in EAC patients compared to age matched healthy controls. Similarly, when mimicking conditions of the TME including nutrient deprivation and hypoxia, this results in a significant ($p < 0.001$) increase in DAMP and ICB expression on CD3,4 and CD8 T cells in the TME when treated with radiation. T-lymphocytes induced by checkpoint blockers plus ionising radiation directly to the tumor resulted in the best repression of tumour growth with 3.6Gy inducing the highest rate of cytolysis ($p < 0.001$). ICB and radiation resulted in reduced cancer cell viability and proliferation.

Conclusion: Fractionated radiation can enhance immunologic function. In combination with ICB, this symbiotic relationship enhances the cytotoxic potential of T lymphocytes with conventional dosing, however, with hypofractionation, this signifies true immunogenicity, and as such this provides a basis for advocating for potential combination strategies with ICB in the multimodal treatment of EAC.

562 THE EFFECT OF IONISING-RADIATION AND THE TUMOUR MICRO-ENVIRONMENT (TME) ON TREATMENT NAIVE ESOPHAGEAL ADENOCARCINOMA PATIENT T CELL FUNCTION AND ACTIVITY.

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There is extensive literature demonstrating CD8+ T cells are essential for initial tumour control following radiation, however, effects are reduced after time due to T cell exhaustion and a lack of release Damage Associated Molecular Patterns (DAMPS) which are essential for anti-tumour immune responses. In vivo, activated T-cells migrate to the tumour site within the field of irradiation, however translational studies on the effects of radiotherapy on T-cell activation, function and activity are lacking.

Methods: EAC patient (n = 6) PBMCs were isolated by density centrifugation in Ficoll Paque. T cells were activated and were irradiated at 1.8Gy, 3.6Gy bolus dosing and fractionation for 72 hrs. A panel of immune checkpoints, DAMPS, activation markers, and cytokines were assessed by flow cytometry. To determine the effect of the TME on T cells, PBMCs were cultured under conditions of nutrient deprivation (No Glucose & No Glutamine) under conditions of normoxia and hypoxia. We then ran the aforementioned panel by flow cytometry. We also activated PBMCs with immune checkpoint blockers to determine its effects on T cell expansion and survival.

Results: 3.6Gy induced a significantly higher expression of DAPMS (Fig 1 $p < 0.001$); Calreticulin and HMGB1, most notably under conditions of nutrient deprivation ($p < 0.001$). Ionising radiation also resulted in an increase in the expression of cytokines and importantly in the context of targeted therapy, IR at both the conventional 1.8Gy and 3.6Gy induced a higher expression of checkpoints PD-1, PD-L1, TIGIT, and TIM-3 ($p < 0.001$). Interestingly, when T cells are activated in the presence of ICB (Atezolizumab, Pembrolizumab, Nivolumab), it increases the rate of T cell expansion, and enhances their survival compared to T cell activated only. ($p < 0.001$).

Conclusion: This work demonstrates the impact of clinically utilised fractions of radiation, and conditions of the TME on T cell function and activity, with improved T cell expansion and survival in the presence of ICB's suggesting it may be a feasible combination therapy as an adjunct to radiotherapy.

565 POST-OPERATIVE WEIGHT LOSS AND OUTCOMES FOLLOWING ESOPHAGECTOMY

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Oesophageal cancer is the 11th most common cancer worldwide, with oesophagectomy remaining the mainstay curative treatment, despite significant associated morbidity and mortality. Postoperative weight loss remains a significant problem and is directly correlated to poor prognosis. Measures such as the Enhanced Recovery After Surgery (ERAS) programme and intraoperative jejunostomy feed have looked to tackle this. This study investigates the impact of these on mortality, length of hospital stay and postoperative weight loss.

Methods: Patients undergoing oesophagectomy between January 1st 2012—December 2014 and 28th October 2015–December 31st 2019 in a national tertiary oesophagogastric unit were included retrospectively. Variables measured included comorbidities, operation, histopathology, weights (pre- and post-operatively), length of hospital stay, postoperative complications and mortality. Pre-operative body weight was measured at elective admission, and further weights were identified from a prospectively maintained database, during further clinic appointments. Other data was collected through patient notes.

Results: 594 patients were included. Mean age at diagnosis was 65.9 years (13–65). Majority of cases were adenocarcinoma (63.3%), with varying stages of disease (TX-4, NX-3). Benign pathology accounted for 8.75% of cases.
Mean weight loss post-oesophagectomy exceeded 10% at 6 months (SD 14.49). Majority (60.1%) of patients were discharged with feeding jejunostomy, and 5.22% of these required this feed to be restarted post-discharge.
Length of stay was mean 16.5 days (SD 22.3). Complications occurred in 68.9% of patients, of which 13.8% were infection driven. Mortality occurred in 26.6% of patients, with 1.83% during hospital admission. 30-day mortality rate was 1.39%.

Conclusion: Failure to thrive and prolonged weight-loss following oesophagectomy can contribute to poor recovery, with associated complications and poor outcomes, including increased length of stay and mortality. Further analysis of data to investigate association between weight loss and poor outcomes for oesophagectomy patients will allow for personalised treatment of high-risk patients, in conjunction with members of the multidisciplinary team, including dieticians.

569 LAPAROSCOPIC REPAIR OF A VOLUMINOUS SYMPTOMATIC HIATAL HERNIA USING AN ABSORBABLE SYNTHETIC MESH

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In symptomatic voluminous paraesophageal hiatal hernias not only a laparoscopic surgical approach, but also the use of mesh can be considered too.
The use of surgical protesis in hiatal henia repair was a debated surgical topic in the last years
A laparoscopic repair of a symptomatic type III hiatal hernia by plastic of the hiatus, fundoplicatio and use of an absorbable glycolic acid/trimethylene carbonate synthetic mesh is showed.

Methods: The patient was a 59 years old male suffering from recurrent aspiration pneumonias. Surgery was performed by a standardized tecnique in a high volume laparoscopic surgical centre. The hernia sac was removed and the plastic of the esophageal hiatus was performed. After the mesh placement a Nissen fundoplicatio was performed. No drain was placed.

Results: In the postoperative period a contrat-soluble swallow was performed and it resulted in a good transit witout any sign of recurrence. The patient was discharged with an appropiate oral intake. One year after surgery the patient is asymptomatic and in good conditions.

Conclusion: A voluminous symptomatic hiatal hernia can be successfully treated in a high-volume and long-term experienced laparoscopic surgical.
The use of an absorbable, handily positionable and synthetic mesh can help to gain a lower rate of recurrence without any risk for the patients.
The technical skill and all the surgical steps never are renounceable because of the presence of the mesh.
Further studies with a longer-term follow-up and a international live debate are necessary.

Video: https://www.dropbox.com/s/384ujzm3rnoqe0a/Hiatal%20Hernia%20Dr.%20Cocozza%20ISDE%202020.mp4?dl=0