according to the National Cancer Institute`s Common Toxicity CriteriaV.5.0 and the postoperative complications were evaluated by Clavien-Dindo Grade Criteria. The primary endpoint was the pCR rate. Tumor Secondary endpoints include major pathological response (MPR) rate, objective response rate (ORR), disease control rate (DCR), incidence of TRAEs and irAEs during preoperative and postoperative treatment period, R0 resection rate, postoperative complications and overall survival (OS) and progression-free survival (PFS).

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P-157 Factors associated with success rates and complications of metal stent insertion for left-sided colorectal cancer obstruction

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Background: There has been increased use of self-expandable metal stents (SEMS) in treating malignant colorectal obstruction (MCO) as a bridge to surgery and palliative treatment. The aim of this study was to investigate factors that are associated with the outcomes of SEMS insertion for left-sided MCO.

Methods: Patients who underwent SEMS insertion for MCO at six hospitals in Honam province of South Korea between 2009 and 2018 were reviewed retrospectively. 696 patients underwent SEMS placement for left-sided MCO and their data were analyzed. Technical success, clinical success, complications, and predictors of outcome were included as main outcome measures.

Results: Technical and clinical success rates were 98.6% (686/696) and 89.2% (621/696), respectively. Complications including stent migration, tumor ingrowth, outgrowth, perforation, bacteremia/fever, and bleeding occurred in 114 (16.4%) patients. BMI was associated with technical success ($P = 0.045$). BMI, length of obstruction, type of stent was associated with clinical success rate ($P = 0.044$, $P = 0.014$, $P < 0.001$, respectively). Stage IV, type of stent was associated with complication rate ($P = 0.007$, $P < 0.001$ respectively) In multivariate regression analyses, BMI was a significant independent predictive factor for the technical success of SEMS placement ($P = 0.045$). Length of obstruction, the use of uncovered stent were significant independent predictive factors for the clinical success of SEMS placement ($P = 0.011$, and $P < 0.001$, respectively). The use of covered stent were significant independent predictive factors for the development of complications after SEMS placement ($P < 0.001$).

Conclusions: Higher BMI was predictive factor for higher technical success rate. Lower length of obstruction, the use of uncovered stent were predictive factor for higher clinical success rate. The use of covered stent was risk factor for development of complications.

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P-158 The algorithm of esophagectomy technique selection in surgical treatment of squamous cell carcinoma and adenocarcinoma of esophagus

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Background: The tasks of surgical treatment include oncological radicality, resectability, safety. Surgical approach and esophagectomy techniques, risks and benefits of lymphadenectomy volume, the need for sufficient clearance from the tumor, the functional and anatomical features of gastric conduit, the advantages and disadvantages of the gastric conduit routes and the level of anastomosis formation, neoadjuvant therapy should be considered.

Methods: The study included 300 cases who experienced extended hybrid or complete minimally invasive esophagectomy with gastric conduit reconstruction. Prospective arm included 119 patients who experienced surgery in 2018-2022 when surgery type selection was worked out by algorithm; retrospective arm included 126 subjects with surgery performed in 2012-2017, when proposed algorithm had not been implemented. The population of the arms was similar by the age, sex, amount, staging, histology, type of surgery ($p>0,05$). The analyzed results were depended on: the surgical approach (minimally invasive, hybrid minimally invasive), esophagectomy technique (by McKeown, Lewis), lymph node dissection volume (2S, 2F, 3F), clearance from the tumor, the width of gastric conduit (wide or narrow), the route of the gastric conduit (retrosternal and right intrapleural), the level of anastomosis formation (neck and pleural cavity, the neoadjuvant therapy program (the fact of radiation therapy). Adverse events were assessed by Katayama-Clavien-Dindo scale.

Results: The algorithm of surgery type selection was worked out. Only the upper thorax esophageal cancer is reasonable for McKeown procedure with cervical anastomosis and narrow gastric conduit. Due to perfusion disorders provoked by radiation therapy and distance from the blood supply point cervical anastomosis leak is a frequent complication but can be cured as salivary fistula after proper drainage. The analyzed data insisted to refuse unreasonable McKeown procedure and narrow gastric conduit formation: 64 procedures performed before the algorithm implementation and only 25 after it. This is one of the reasons in anastomotic leak rate decrease. The middle thorax esophageal cancer should be operated by Lewis procedure with anastomosis in thoracic aperture with wide gastric conduit. Lower thorax cancer is also operated with Lewis procedure, but anastomosis should be formed at the level of tracheal bifurcation. Abdominal and cardioesophageal cancer require resection of small curvature with anastomosis formed below tracheal bifurcation. R0 resection rate achieved 99 % in algorithm group and 98 % in the group without algorithmic surgery tactic selection ($p>0,05$). Postoperative mortality reduced from 11,5 % in 2012-2017 to 5,9 % ($p < 0,05$). Anastomotic leakage decreased from 19,8 % with 7,1 % mortality rate among the cases of the retrospective group to 13,4 % with 4,2 % mortality rate among the cases of the prospective group ($p < 0,05$). The overall complication rate measured by Katayama-Clavien-Dindo scale becomes less with percentage 56 % and 45,5 % respectively ($p < 0,05$). There was no statistical validity achieved in comparison of recurrence free survival and overall survival between arms grouped by the stage respectively.

Conclusions: The implementation of the algorithm improves the results of surgical treatment of the esophageal cancer. It brought the reduction of general and esophagectomy-specific postoperative complications, especially anastomotic leakage, postoperative mortality, also brought the increase of oncological radicality.

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P-159 Association of acrochordons and colorectal polyps: A pilot study to identify potential genetic or viral etiology

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Background: Several reports suggest that skin papilloma may be a marker for the presence of colonic adenomatous polyps. Since colorectal neoplasms have polyps as precancerous lesions, a strong correlation between the lesions could identify the right profile for the patient who could become the candidate for personalized screening for colon cancer. Despite the inconclusive data, no research was conducted to analyze the genome of lesions by techniques such as Next Generation Sequencing (NGS). The aim of our work was to be the first study to analyze biopsies from adenomatous polyps and acrochordons identified in the same patients, and also to determine any viral inclusions or potentially common driver mutations.

Methods: In this pilot study, human papillomavirus (HPV) testing was done for low-risk and medium-risk subtypes. For both categories of subjects, NGS testing was chosen and a complete evaluation of 15 genes that are frequently mutated in solid tumors was carried out.

Results: A total of five patients were included in the study, four of whom were male. None of them had no digestive symptoms at baseline. On average, 4 biopsies of skin papilloma and 4 biopsies of colonic polyps were taken. If the patient had more than 4 lesions, the most relevant was chosen. DNA extraction was performed from paraffin embedded tissue with ReliaPrep ™ FFPE gDNA Miniprep System - Promega, and from colorectal polyps with the Wizard® Genomic DNA Purification Kit — Promega, in accordance to producer indications.[BG1] HPV testing was performed using the HIGH + LOW PAPILLOMASTRIP - PAPILLOMAVIRUS kit from OPERON, which can identify the following subtypes: Medium-high risk: 16, 18, 26, 31, 33, 35, 39, 45, 51, 52, 53, 56, 58, 59, 66, 68, 69, 73 and 82 (MM4 and IS39[BG2]) and Low risk: 6, 11, 40, 42, 43, 44, 54, 61, 62, 67, 70, 71, 72, 74, 81, 83, 84 and 91. For the same samples NGS testing was performed using the TruSightTumor 15 panel (TST15) from Illumina. Target genes were AKT1, GNA11, NRAS, BRAF, GNAQ, PDGFRA, EGFR, KIT, PIK3CA, ERBB2, KRAS, RET, FOXL2, MET, TP53.

Conclusions: In this small cohort of patients, no associations between acrochordons and colorectal polyps in terms of viral or genetic etiology were identified. An extensive investigation of several other predictors for colonic polyps may be valuable in detecting early carcinogenesis. These could help for future guidance in building effective screening programs, which is critical in preventing unnecessary patient morbidity and mortality.

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P-160 Mismatch repair system protein deficiency as a resistance factor for locally advanced rectal adenocarcinoma patients receiving neoadjuvant chemo-radiotherapy

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Background: In rectal cancer, available data on Mismatch Repair system deficit and microsatellite instability are conflicting and are generally derived from a small number of patients due to the rarity of this condition. Our study aimed to evaluate the frequency and therapeutic implications of Mismatch Repair proteins (MMR) status in patients affected by locally advanced rectal cancer.

Methods: We retrospectively collected data from 318 patients affected by locally advanced rectal cancer (LARC) (cT3-4 +/- N1-2) treated at the Medical Oncology Unit of the University Hospital of Cagliari, Italy, the Medical Oncology Department, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy and at the Medical Oncology Unit, AOU Ospedali Riuniti, Ancona. Italy. All patients included in the study underwent neoadjuvant concurrent capecitabine and long-course radiotherapy (RT) (total dose of Gy 50.4), then a total mesorectal excision (TME) was performed. MMR expression was evaluated through immunohistochemistry. Primary objective was major TRG (0-1 Ryan's score) while secondary objectives were pathological complete response, disease-free survival (DFS) and overall survival (OS).

Results: 160 patients (148 pMMR and 12 dMMR) were included in the exploratory cohort and 158 (146 pMMR and 12 dMMR) were included in the validation cohort. A major TRG has been shown in 64/148 (42,6%) and 63/146 (43,1%) patients with pMMR in exploratory cohort and validation cohort, respectively; while no major TRG have been shown in dMMR patients in exploratory cohort nor in validation cohort. Both exploratory and validation cohorts showed a statistically significant higher median DFS in pMMR patients compared to dMMR ones: NR vs 14 months in exploratory cohort ($p = 0,003$) and NR vs 17 months in validation cohort ($p = 0,02$).

Conclusions: Our retrospective study indicated an association between dMMR and poor or no response to preoperative chemoradiotherapy. These results are consistent with the role of MMR as a predictor of poor-response to chemoradiotherapy and represent a hypothesis-generating study for the selection of these patients for immunotherapy in the neoadjuvant setting, in which the available data are promising.

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P-161 MiR181c/d regulates sensitivity to cisplatin/gemcitabine by targeting SIRT1 in cholangiocarcinoma

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Background: Despite recent advances, cholangiocarcinoma (CCA) remains one of the most lethal tumour worldwide due to late diagnosis and resistance to conventional therapies. There is an unmet need for novel therapeutics as well as novel prognostic and predicitve biomarkers. In recent years, high-throughput technologies have enabled extensive genome, exome, and transcriptome sequencing unveiling, among others, the regulatory potential of microRNAs (miRNAs). Compelling evidence have demonstrated that various miRNAs are dysregulated in CCA, promoting cholangiocarcinogenesis and tumor progression.

Methods: We performed SmallRNASeq transcriptomics on resected specimens of 62 CCAs undergoing curative-intent surgery at the University Hospital of Modena (Italy). MicroRNA expression levels were evaluated in a panel of CCA cell lines (SNU_308; KMCH1; EGI; TFK1; SNU_1079; HUCCT1; RBE; KKM156) and 2 lines of normal cholangiocytes (H69; NHC) by qPCR analysis. CCA cell lines were transiently transfected with inhibitors and/or mimics of miR-181c/d and cell viability was assessed by MTT assay in presence and/or absence of Cisplatin/Gemcitabine at different doses. Clonogenicity and chemosensitivity were evaluated in colony formation assays in presence and/or absence of treatment. Bioinformatic analysis identified candidate targets of miR-181c/d. Effects of miR-181c/d modulation on target expression was evaluated by qPCR analysis and Western Blotting.

Results: High-throughput analysis successfully identified miR-181c and -181d as significantly downregulated in CCA patients. Interestingly, low miR-181c and -181d expression levels were correlated with a worse prognosis and lack of efficacy of treatments. In fact, relapse-free survival was significantly shorter in miR-181c/d low expressing patients ($P = 0.02$); moreover, miR-181c/d expression was downregulated in patients with progressive disease ($P = 0.005$). To confirm this evidence, we analyzed CCA cell lines by qPCR and we verified that both miRNAs were dysregulated. Then, we performed functional in vitro experiments in CCA cell lines transiently transfected with inhibitors and/or mimics of miR-181c/d. Our goal was to evaluate if the modulation of both miRNAs could have anti-tumor activity. Cell viability was assessed by MTT assay in presence and/or absence of treatment. Overexpression of miR-181c/d affected cell viability and increased sensitivity to chemotherapy compared to controls. Furthermore, we performed colony formation assays to confirm the impact on cell proliferation and chemosensitivity in presence and/or absence of treatment. Overexpression of miR-181c/d reduced the number of colonies and counteracted chemoresistance. In addition, by using bioinformatic tools we showed that the miR-181c/d functional role is determined by binding to their target SIRT1 (Sirtuin 1). We evaluated the effects of miR-181c and -181d modulation on SIRT1 expression levels by performing qPCR analysis and Western Blotting. Overexpression of miR-181c/d caused SIRT1 downregulation.

Conclusions: To our knowledge, this is the first study to reveal the potential for miR-181c/d as tumor suppressor miRNA in CCA. The downregulation of miR-181c/d correlated with a significantly poorer prognosis in CCA patients and the overexpression of miR-181c and -181d reduced tumor growth in CCA cell lines and increased sensitivity to chemotherapy through the targeting of the histone deacetylase SIRT1. Although these preliminary data are in need of confirmatory analysis and validation, miR-181c/d may represent a useful biomarker to monitor and predict response to treatment in CCA patients.

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