

Results: In univariate and multivariate analysis no single clinical variable came out as a specific factor predicting CD related complications of the pouch, and no single histological item was found to be a specific hallmark for CD related complications of the pouch. By using a ROC curve, a cut-off value of 10 was found with a specificity of 88.2% and a sensitivity of 43.4% for the diagnosis of CD related complications of the pouch. The Positive Predictive Value (PPV) for this test was 83.3% and the Negative Predictive Value (NPV) was 53.6%.

Conclusions: No single histological item was found to be a specific hallmark for CD related complications of the pouch. A cut-off of 10 on the histological Heidelberg Pouchitis Activity Score showed a high specificity and PPV for the diagnosis of CD related complication of the pouch. This cut-off should be validated in a large prospective study.

R05

Prognostic impact of quality control of total mesorectal excision specimen evaluation

P. DEMETTER (1), A. JOURET-MOURIN (2), C. SEMPoux (2), A. HOORENS (3), N. NAGY (4), C. CUVELIER (5), T. VANDENDAEL (6), N. VAN DAMME (6), G. SILVERSMIT (6), F. PENNINCKX (7) / [1] Erasme University Hospital, Anderlecht, Belgium, Pathology, [2] Cliniques Universitaires Saint-Luc, Brussels, Belgium, , Belgium, Pathology, [3] UZ Brussel, Jette, Belgium, Pathology, [4] CHU, Charleroi, Belgium, Pathology, [5] UZ Gent, Gent, Belgium, Pathology, [6] , , [7] UZ Leuven Gasthuisberg, Leuven, Belgium, Abdominal Surgery

Introduction: In order to audit the quality of total mesorectal excision (TME), a central pathology review has been organised within the framework of the Belgian PROCARE (Project on Cancer of the Rectum) project. A fair to moderate concordance in interpretation of the TME plane by local pathologists, sensibilised for the aims and procedures of PROCARE by workshops and communications at national meetings, and the review panel has been observed.

Aim: We wanted to explore the potential impact of TME grading by an expert panel on oncological outcome.

Methods: Based on photographic material, TME quality was reviewed in 482 patients. For the present study, 53 patients with a stage IV tumour and 2 patients with unknown incidence date were excluded, resulting in a study population of 427 patients. Quality assessment was based on the classic three-graded score: mesorectal, intramesorectal and muscularis propria resection. Both local and expert panel TME quality grading were used as predictors in univariable Cox regression models for 4 outcome variables: local recurrence, distant metastasis, overall survival and disease-free survival. Prediction error differences between local and expert grading were tested using the method of van de Wiel (van de Wiel et al, Biostatistics 2009). Brier scores at 1, 3 and 5 years for both predictors were used as a measure for the prediction error.

Results: Resection planes were concordant in 238 cases (56%). Downgrading from mesorectal to muscularis propria resection was noted in 28 cases (7%). There were no significant differences in the prediction error between the two models; both local and expert TME quality grading predicted equally well the outcome variables.

Conclusions: Grades of TME quality as reported by local pathologists can be used for outcome analysis. Differences in judgement of the TME resection plane are limited and do not have a significant impact on predicting the oncological outcome of a patient cohort. Quality control of TME assessment does not seem to be warranted in the context of improvement projects if pathologists are adequately trained.

R06

Preoperative treatment modifies the immune microenvironnement of liver colorectal metastases.

M. VANDENEYNDE (1), B. MLECNIK (2), J. MACHIELS (3), D. DEBETANCOURT (4), G. BINDEA (2), G. PAIRET (5), A. JOURET-MOURIN (5), C. SEMPOUX (5), J. GIGOT (6), C. HUBERT (6), Y. HUMBLET (3), J. CARRASCO (7), N. HAICHEUR (8), F. MARLIOT (8), F. PAGÈS (8), J. GALON (2) / [1] Cliniques Universitaires Saint Luc, , Belgium, Gastroenterology, oncology, [2] Centre de Recherche des Cordeliers, Paris, France, , [3] Cliniques Universitaires Saint Luc, , Belgium, Oncology, [4] Cliniques Universitaires Saint Luc, , Belgium, Centre du cancer, [5] Cliniques Universitaires Saint Luc, , Belgium, Pathology, [6] Cliniques Universitaires Saint Luc, , Belgium, Hepato-bilio-pancreatic surgery, [7] Grand Hopital de Charleroi, Charleroi, Belgium, Oncology, [8] Hôpital Européen Georges Pompidou, Paris, France, Immunology

Introduction: We previously reported that an adaptive Th1 immune response (CD3/CD8/CD45RO T-cells) observed in resected primary colorectal tumor and liver colorectal metastases (LCM) is an important prognostic factor. B and FoxP3 regulatory lymphocytes participate to the modulation of this response.

Aim: We aimed to investigate whether the preoperative treatments influenced the quality and the density of the immune infiltrates previously reported in the LCM.

Methods: We used a cohort of metastatic colorectal patients (n=107) engaged for curative liver surgery with available FFPE blocks for all resected LCM to confirm the prognostic impact of the immune response. Among this cohort of 338 LCMs, 46 were completely resected after chemotherapy (CT) alone, 130 after CT + anti-VEGF, 118 after CT + anti-EGFR and 44 after surgery alone. LCMs were analyzed for histological response according the Tumor Regression Grade (TRG) and regrouped as Response (R, TRG1-3) or No Response (NR, TRG4-5). The density of CD3+ (T-cells), CD8+ (cytotoxic), CD45RO+ (memory), CD20+ (B-cells) and FoxP3+ (regulatory) in the core (CT) and invasive margin (IM) of all LCM was quantified on immunostained slides. The mean density value (CT/IM) was calculated for each marker with a dedicated image analysis software on whole-slide imaging. Comparisons were made using the Wilcoxon-Mann-Whitney test.

Results: LCMs showing R (compared to NR and untreated LCM) were more frequently associated with a high immune infiltrate for CD3+ (CT: $p<0.005$; IM: $p<0.05$), CD8+ (CT: $p<0.005$; IM: $p<0.005$) and CD20+ (CT: $p<0.05$). Conversely, high FoxP3+ density in the CT and IM was related to NR and untreated LCMs ($p<0.01$). LCMs treated with an anti-EGFR therapy showed higher densities of CD3+ (CT: $p<0.005$; IM: $p<0.01$), CD8+ (CT: $p<0.005$), CD45RO+ (CT: $p<0.005$), CD20+ (CT: $p<0.005$) and FoxP3+ (CT: $p<0.05$; IM: $p<0.005$) compared to other treatments and untreated LCMs.

Conclusions: Preoperative treatment modifies the LCM immune microenvironnement. LCMs with a histological response show a cytotoxic immune response (CD3+/CD8+) with associated B-cells (CD20+) and downregulated Tregs (FoxP3+). The use of an anti-EGFR therapy significantly increases immune infiltration in the CT.

R07

Genetic dissimilarity between primary colorectal carcinoma and their lymph node metastases: ploidy, p53, bcl-2 and c-myc expression

A. FODA (1), K. ZALATA (1), M. ELSHAL (2) / [1] Mansoura Gastroenterology Center, Mansoura, Egypt, Pathology department, [2] Sadat City University, , Egypt, Molecular biology department, Genetic Engineering and Biotechnology Institute

Introduction: The current paradigm of metastasis proposes that rare cells within primary tumors acquire metastatic capability via sequential mutations, suggesting that metastases are