- D07 -

State-of-the-art Lecture

The role of the gut microbiome in gastrointestinal and liver disease.

N. Delzenne, UCL, Belgium.

- D08 -

PROGNOSTIC VALUE OF FDG PET/CT IN LIVER TRANSPLANTATION FOR HEPATOCARCINOMA.

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Aim : FDG uptake has been shown to predict the outcome in large series of patients with hepatocarcinoma (HCC) in Asia, but few data are available regarding European populations. Our aim was to evaluate the prognostic value of pre-treatment FDG PET-CT in patients treated by liver transplantation.

Methods : We retrospectively analyzed the data of 27 patients (24 M and 3 W, mean age 58 ± 9 years). The mean follow-up was 26 ± 18 months (min 1 month, max 66 months). All patients had an FDG PET-CT before the transplantation. The FDG PET/CT was performed according to a standard clinical protocol : 4 MBqFDG/kg body weight, uptake 60 min., low-dose non-enhanced CT. We measured the SUVmax and SUVmean of the tumor and the normal liver. The tumor/liver activity ratios (RSUVmax and RSUVmean) were tested as prognostic factors and compared to the following conventional prognostic factors : MILAN, CLIP, OKUDA, TNM stage, alphafoetoprotein level, portal thrombosis, size of the largest nodule, tumor differentiation, microvascular invasion, underlying cirrhosis and liver function.

Results : The DFS was 87.2% at 1y and 72.1% at 3y. The OS was 85.2% at 1y and 80.7% at 3y. According to an univariate Cox model, RSUVmax, RSUVmean and healthy liver were predictors of DFS and RSUVmax, RSUVmean, size of the largest nodule, CLIP, liver involvement > 50%, and healthy liver predicted the OS. According to a multivariate Cox model, only RSUVmax predicted DFS and RSUVmax and liver involvement > 50% predicted OS. An ROC analysis of the ratios showed that the 1.15 cut-off for RSUVmax was best for predicting both the DFS (Cox regression : HR 14.4, $p = 0.02$) and OS (HR 5.6, $p = 0.049$). The Kaplan-Meier curves and Logrank tests confirmed those results. Even though the MILAN criteria alone were not predictive, it is worth noting that none of the patients outside the MILAN criteria and with RSUVmax < 1.15 relapsed.

Conclusions : The RSUVmax is a strong prognostic factor for recurrence and death in patients with HCC treated by liver transplantation with a cut-off value of 1,15. further prospective studies should test whether the metabolic index should be systematically included in the preoperative assessment.

- D09 -

PREOP. CHEMOSENSITIVITY TESTING AS PREDICTOR OF ADJUVANT BENEFIT IN STAGE III COLON CANCER (PEPITA).

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Introduction : Adjuvant chemotherapy improves stage III colon cancer outcome but is not effective for all patients. PePiTA trial's main hypothesis is that the absence of metabolic response of the primary tumor after 1 preoperative chemotherapy course predicts the absence of benefit from adjuvant chemotherapy (at 3-year DFS). This strategy's aim is to spare patients from useless toxicities, improve healthcare resource allocation, and guide translational research. This interim analysis was performed for safety and feasibility of Metabolic Response Assessment (MRA).

Methods : Patients ≥ 18 years, with PS ≤ 1, diagnosed with colon cancer considered for curative resection are eligible, after signed consent. Baseline PET is repeated after 1 chemotherapy cycle, followed by surgery. PET quality insurance and MRA are performed centrally and the result is blinded for investigators.

Results : From 2010 to 2013, 114 patients – M/F (55%/45%), median age 66 (26-81), ECOG 0/1(92%/8%) – were included in 15 Belgian centers. 11 patients were excluded from analysis : 2 hyperglycemia at baseline PET ; 2 withdrew consent ; 6 PET-revealed stage IV CC ; and 1 second cancer. Preoperative CT was associated with 5% grade 3-4 neutropenia, 1% grade 3 diarrhea, 1% grade 3 hypokaliemia, 1% peritonitis and 1% grade 3 thromboembolic events. Colectomies were performed in all patients after a median of 20 days (interquartile interval 18-21) : 32 right (31%), 69 left (67%), and 2 procedures not detailed. Pathology showed stages 0 (1%), I (13%), II (34%), III (47%), IV (7%), without lymph node downstaging. Postoperative morbidity is 9% (95%CI 5-16%) and includes fistulas (4%), transient ischemic attack (1%), ileus (2%), and evisceration (1%), but no death. Technical or methodological reasons prevented MRA in 19/103 pts. Median SUVmax was 14.4 (4.9-47.8) at baseline, and 10.9 (0-39.3) on day 14. 2 patients presented with complete MR. For the others, median delta SUVmax was -22% (-60 to +31%). MR was observed in 60% of patients, and was absent in 40%, with equal distribution for stages II and III (p = 1.00).
Conclusions : 1 course of chemotherapy is feasible before curative surgery for colon cancer, without inducing excessive toxicity, delay or surgical morbidity. MRA indicated metabolic signs of chemoresistance in 40% of the primary tumors.

- D10 -

PRE-OPERATIVE SEROLOGICAL MARKERS MAY PREDICT POSTOPERATIVE CROHN'S DISEASE RECURRENCE. M. Noben (1), A. De Buck Van Overstraeten (2), S. Lockton (3), G. De Hertogh (2), F. Princen (3), A. Wolthuis (2), G. Van Assche (2), S. Vermeire (2), S. Singh (3), A. D'hoore (2), M. Ferrante (2). (1) Translational Research Center for Gastrointestinal Disorders (TARGID), KULeuven, Leuven, Belgium ; (2) University Hospitals Leuven, Leuven, Belgium ; (3) Prometheus Laboratories Inc., San Diego, United States.

Introduction : Preventing postoperative endoscopic (ER) and clinical recurrence (CR) remains a challenging issue in patients with Crohn's disease (CD) undergoing an intestinal resection. Several clinical and histological risk factors have been identified, and may guide selection of appropriate candidates for postoperative prophylactic CD therapy.
Aim : We evaluated if a set of pre-operative serological markers could strengthen the prediction of postoperative ER and CR.
Methods : Our study population consisted of 100 consecutive patients (41 males, 27 active smokers, median age 41.7 years) undergoing an ileal resection with ileocolonic anastomosis for refractory CD, in whom a serum sample was collected ≤ 1 week prior to surgery. All patients were followed prospectively and underwent a postoperative endoscopic evaluation at 6 months. The primary endpoint (ER) was defined as a postoperative endoscopic recurrence score of i3 or i4. Secondary endpoints included time to clinical recurrence. Sera were analysed blindly at Prometheus laboratories for the expression of anti-*Saccharomyces cerevisiae* IgA (ASCA A) and IgG antibodies (ASCA G), three different anti-flagellin antibodies (CBir1, Fla2 and FlaX), antibodies to the outer-membrane porin C of *Escherichia coli* (OmpC), and atypical perinuclear antineutrophilic cytoplasmic antibodies (pANCA). The Q3 value of each individual marker in this dataset was defined as the cut-off point. Predictors of both ER and CR in univariate analyses were included in the binary logistic and Cox regression analysis.
Results : Twenty-five patients developed ER at 6 months. Fla2 > 66 EU and active smoking were independently associated with ER (Table 1). During a median follow-up of 23.6 months, 29 patients developed a CR, with Fla2 > 66 EU, pANCA positivity and active smoking as independent risk factors (Table 1). A cumulative risk score was developed by combining 3 risk factors (Fla2 > 66 EU, pANCA positivity, and active smoking). Based on this cumulative risk score, we could observe a significant and gradual increased risk of both ER (Figure 1, linear-by-linear $p < 0.001$) and CR (Figure 2, LogRank $p < 0.001$).

Table 1. — Multivariate analysis

	Endoscopic recurrence * (Logistic Regression)	Clinical recurrence * (Cox Regression)
Fla2 > 66 EU	3.0 (1.1-8.7) p = 0.037	2.2 (1.0-4.6) p = 0.041
pANCA positive	2.7 (0.9-8.1) p = 0.083	2.5 (1.2-5.4) p = 0.016
Active smoking	3.1 (1.1-8.8) p = 0.029	2.6 (1.2-5.5) p = 0.011

* Odds ratio (95% confidence interval).