

potential parameters for nodal involvement were collected using standardized documentation forms; surgical complications, mortality and disease-free survival were obtained by a central registry. The starting date of follow-up of each patient began at screening colonoscopy.

Results: 180 pT1 tumors were diagnosed, 140 (77.8%) were completely removed by endoscopy (en-bloc = 80.0%, piecemeal = 20.0%), the remaining 40 (22.2%) were biopsied and referred to surgery. Out of 140 malignant adenomas endoscopically removed, 94 (67.1%) underwent resective surgery, 3 of them (3.2%, all with high-risk adenomas) showed nodal involvement compared with 3/40 (7.5%) directly sent to surgeon. Out of 24 patients with low-risk adenomas, 7 (29.2%) underwent surgery; no metastatic nodes were found. Surgical complications were observed in 15.8% patients. Among 145 patients followed up for at least 36 months (median = 78; 10-90 percentile: 43-152), 5 (5.12*1000 PY) died for their neoplastic disease and 2 showed disease progression; out of 142 patients with Dukes A neoplasia, 4 (4.19*1000 PY, all of them underwent surgery) died due to colon cancer and 2 showed disease progression. Regarding histologic and therapeutic quality indicators, the number of removed nodes during surgery was <7 in 59 patients (44.4%), histologic description of endoscopically removed adenomas was considered complete in 88.9% of cases, a second pathologic opinion was requested in 24.4% of patients.

Conclusions: Nodal metastatic risk in colon pT1 tumors is well predicted by known histologic factors even in a screening scenario. However, surgical overtreatment is still significantly present and there is ample room for improvement regarding diagnostic and therapeutic flow-chart.

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PHENOTYPE OF TWO ITALIAN LYNCH SYNDROME FAMILIES WITH EPCAM DELETIONS

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Background and aim: Lynch Syndrome (LS) is caused by constitutional mutations in Mismatch Repair genes, but it can also be due to heritable epimutations of the same genes. The genetic basis of constitutional MSH2 promoter methylation has been clarified to be caused by deletion of distal region of EPCAM, a gene located upstream the MSH2 locus. EPCAM deletions, leaving intact the MSH2 gene, are responsible of transcriptional read-through, with production of fusion EPCAM/MSH2 transcripts. This deletion results in inherited allele-specific methylation of MSH2 promoter and gene silencing with a colon-specific phenotype.

Material and methods: Out of 38 Lynch families followed at our Institution, 2 families (5.2%) displayed MSH2-negative immunohistochemistry with EPCAM mutations. EPCAM deletion screening was performed by MLPA (Multiplex Ligation-Dependent Probe Amplification) and long-range PCR across the deletion was applied to identify the exact breakpoints. PCR products were sequenced at various positions in both orientations. Methylation analysis was performed by SALSA MS-MLPA Mismatch Repair genes using DNA isolated from formalin fixed paraffin embedded material.

Results: EPCAM deletions were: span 4.9kb including exons 8-9 in one family and 16.6kb including exons 5-9 in the others. The breakpoints have been characterized, confirming that both large deletions are caused by non-allelic homologous recombination events between Alu elements with high inter-homology located in intronic and intergenic regions. In one patient with the larger deletion we showed that in colorectal tissue deletion leads to hypermethylation of MSH2 promoter, production of different out-of-frame and in-frame fusion EPCAM/MSH2 transcripts and loss of nuclear expression of MSH2 protein. Six members of the 2 EPCAM families are in follow-up. The clinical phenotype was characterized by early colo-rectal cancer (CRC) onset (mean 37 years, range 25–46) and multiple CRCs (up to 4 cancers despite colonoscopy surveillance). The first CRC diagnosed in 4 patients out of 5 was at the rectum. 1 patient developed duodenal carcinoma as extra-colonic cancer (EXC).

Conclusions: The phenotype of LS patients, carrying EPCAM deletions, was characterized by multiple primary cancers at colon-rectum with rectal cancer as the first tumor diagnosed. EXCs were observed suggesting the surveillance should not be focused only on CRC.

P.13.5

COLORECTAL CANCER IN PATIENTS WITH TYPE 2 DIABETES MELLITUS: PRELIMINARY RESULTS FROM AN ONGOING CASE-CONTROL STUDY

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Background and aim: Understanding the risk factors for Colorectal cancer (CRC) is crucial to the development of effective strategies for its prevention. Meta-analysis and epidemiological studies have already shown that Type 2 diabetes mellitus (DM) is associated with an increased risk of CRC and have provided data to support a positive relationship between these diseases.

Material and methods: We retrospectively evaluated 741 consecutive Caucasian patients with type 2 DM who underwent colonoscopic screening for colorectal cancer and followed in our tertiary referral center in 2000-08 for the incidence of CRC. Patients were stratified based on gender, age, body mass index (BMI), alcohol and NSAIDs assumption, family history for cancer, blood glycosylated hemoglobin levels, hypertension, hypertriglyceridemia, age at diabetes onset and duration, treatment with insulin or other hypoglycemic drugs. A total of 257 consecutive control patients were selected from a cohort of patients followed as outpatients for thyroid diseases.

Results: At a median follow up of 132.5 months (range 33.3–175.7) 56 cases of cancer (prevalence 7,56%) occurred; among these, 14 cases of CRC were reported (prevalence 1,88%) among the diabetic patients, while only one case (prevalence 0,004%) occurred in the control group, although this difference is not statistically significant (chi-square 2,9, p=0,08). Median duration of DM to CRC diagnosis was 156 months (range 1–768). At the univariate analysis older age (p=0.001), and diabetes duration (p=0.001) were related to higher risk of cancer, while metformin seems to be protective towards cancer (p=0.058). In the subset of patients with CRC, older age (p=0.001) and diabetes duration (p=0.001) were related to higher risk of CRC, such as treatment with sulphonylureas (p=0.01).

Conclusions: Our preliminary data show that the prevalence of CRC in the cohort of patients with type 2 DM was higher compared to that from our control group, and to that from the National Tumor Register up 2010 (0,5%). Furthermore we could interestingly hypothesize that sulphonylureas may play a role in CRC carcinogenesis altering the physiological insulin secretion.

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WAITING TIME AT WAITING ROOM: THE IMPACT ON TOLERANCE DURING UPPER ENDOSCOPY

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Background and aim: Esophagogastroduodenoscopy (EGD), even if it is an invasive procedure, is an essential and very commonly used procedure for the evaluation of a multitude of gastrointestinal (GI) symptoms. Although it is increasingly required, the benefit of sedative premedication remains controversial. The same way, the influence of the time interval between arrival at the endoscopic suite and the effective endoscopic examination, is not clear. Our study assesses the waiting time impact on tolerance during upper endoscopy.

Material and methods: Our study included consecutive outpatients undergoing diagnostic EGD for various indications. Sex, age, BMI, previous endoscopic experiences, antidepressant therapy and the waiting time were recorded. Anxiety before the procedure was rated on an ascending scale from 0 to 10 (0 = no anxious to 10 = extremely anxious). After the procedure was concluded, patients were monitored in the recovery room. Afterwards, a questionnaire was filled in by the participants to determine pain and discomfort to the procedure based on a scale from 1 to 10 (0 = no pain/discomfort encountered to 10 = extremely painful/uncomfortable).

Results: 80 (32 males; mean age 57.2 years) consecutive outpatients were