Gut-IDDF 2018 Best Abstracts

Basic Gastroenterology

IDDF2018-ABS-0123

NOVEL MODALITY OF NON-INVASIVE COLORECTAL CANCER SCREENING: COMBINATION OF FAECAL CYCLOOXYGENASE 2 (COX-2) MRNA, CARCINOEMBRYONIC ANTIGEN (CEA), AND FAECAL IMMUNOCHEMICAL TEST (FIT)

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10.1136/gutjnl-2018-IDDFbestabstracts.1

Background Colorectal is the third most commonly occurring cancer in men and the second most commonly occurring cancer in women. Screening modalities and guidelines directed at prevention and early detection have progressed and resulted in a significant decrease in the prevalence and mortality of colorectal cancer via direct visualisation or using specific markers. Noninvasive screening modalities are continuously being studied. Identification of specific genetic alterations and biomarkers in the adenoma-cancer sequence allow for the study and development of noninvasive screening modalities beyond guaiac-based faecal occult blood testing. The purpose of this study is to highlight some of the new candidate predictive and prognostic colorectal cancer molecular markers for stool samples.

Methods A cross-sectional study was conducted at Ciptomangunkusumo Hospital patients underwent colonoscopy and biopsy for advanced precancerous lesion and colorectal cancer; stool samples were also obtained from the patients. We compared noninvasive test from stool sample using faecal immunochemical test (FIT), KRAS, Carcinoembryonic Antigen (CEA), Cyclooxygenase 2 (COX-2) mRNA, M2-Pyruvate Kinase (M2-PK), calprotectin and its combination in persons at average risk for colorectal cancer.

Results 97 patients with mean age 56 years old (deviation standard ± 11.9). The proportion of female 47.4% (n=46), and male 52.6% (n=51). The proportion of colorectal cancer patients were 15.5%, advanced precancerous lesions were 24.7%. Combination of faecal COX2-CEA-FIT yields the highest sensitivity score. The sensitivity for detecting colorectal cancer was 93.3% with combination of faecal COX2-CEA-FIT. The sensitivity for detecting advanced precancerous lesions was 75% with combination of faecal COX2-CEA-FIT. Specificities with combination of COX2-CEA-FIT for detecting colorectal cancer was 61.3%. Specificities with combination of COX2-CEA-FIT for detecting advanced precancerous lesions was 62%. AUC score for discriminating colorectal cancer was 77.3% (CI 66.4%–88.2%), while AUC score for discriminating advanced precancerous lesions was 68.5% (CI 56.4%–80.6%). PPV 31.1%, NPV 98% LR+2.41, LR- 0.11 for discriminating colorectal cancer; while PPV 40%, NPV 88%, LR+1.97, LR- 0.4 for discriminating advanced precancerous lesions.

Conclusions Faecal COX2-CEA-FIT yields a high sensitivity rate for screening colorectal cancer.

IDDF2018-ABS-0163

PANCREATIC JUICE MUTATION CONCENTRATIONS CAN HELP PREDICT THE GRADE OF DYSPLASIA IN PATIENTS UNDERGOING PANCREATIC SURVEILLANCE

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10.1136/gutjnl-2018-IDDFbestabstracts.2

Background The measurement of mutations in pancreatic juice samples collected from the duodenum during endoscopic ultrasound (EUS) may improve the diagnostic evaluation of patients undergoing pancreatic surveillance. Our aim was to evaluate the accuracy of using pancreatic juice mutation concentrations to predict the presence and histologic grade of neoplasia in the pancreas.

Methods Digital next-generation sequencing (NGS) of pancreatic juice DNA using a targeted 12-gene panel was performed on 67 patients undergoing pancreatic evaluation during EUS at Johns Hopkins Hospital including patients with pancreatic ductal adenocarcinoma, patients who subsequently underwent pancreatic resection for precursor lesions, patients undergoing surveillance for their familial/inheritable susceptibility to pancreatic cancer, and normal pancreas disease controls.

Results One hundred fifty-five unique somatic mutations were detected after filtering based on the in-house developed algorithm. The most commonly mutated genes after KRAS and GNAS were in descending order of prevalence in TP53, RNF43, SMAD4, ARID1A, CDKN2A, FDXB7 and TGFBR2. Pancreatic juice mutations were detected in all 14 cases with pancreatic cancer, 12 of 13 (92.3%) cases with suspected precancerous lesions, 23 of the 31 high-risk individuals (74.2%) and 4 of 9 disease controls with a normal pancreas. Patients with pancreatic cancer or high-grade dysplasia as their highest grade lesion had significantly higher pancreatic juice mutation concentrations than all other subjects (mean/s.d. digital NGS score; 46.6 ± 69.7 vs. 6.2 ± 11.6 , $p=0.02$). Pancreatic juice mutation concentrations distinguished patients with pancreatic cancer or high-grade dysplasia in their resection specimen from all other subjects with a sensitivity, 72.2%, specificity, 89.4% (area under the curve, AUC 0.872). Mutant TP53/SMAD4 concentrations could distinguish patients with pancreatic cancer or high-grade dysplasia in their resection specimen, from all other subjects with 61.1% sensitivity, 95.7% specificity (AUC 0.819). Among 31 high-risk individuals under surveillance, 2 of the 3 individuals with most abnormal pancreatic juice mutation profiles also had the most abnormalities on pancreatic imaging.

Conclusions Pancreatic juice mutation analysis using digital NGS has potential diagnostic utility in the evaluation of patients undergoing pancreatic surveillance.

IDDF2018-ABS-0178

CONSTRUCTION OF COLORECTAL CANCER SUBTYPES BASED ON STROMA-SPECIFIC GENE EXPRESSION AND PREDICTION OF DRUG RESPONSE

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10.1136/gutjnl-2018-IDDFbestabstracts.3