Advanced Neoplasia Detection in Colorectal Cancer Screening Using Multiple Stool DNA Markers and Haemoglobin


Purpose of the study: Molecular tests have the potential to improve current non-invasive faecal immunochemical test (FIT) screening for colorectal cancer (CRC) and advanced precancerous lesions. We examined the performance of a panel of faecal DNA (sDNA) markers and FIT in archival samples from an invitational CRC screening population.

Methods: Whole stool samples were prospectively collected from individuals participating in an invitational primary colonoscopy-screening program (COCOS trial). Only participants that provided stool, performed FIT (OC-Sensor) and underwent colonoscopy were selected. The sDNA panel included quantitative molecular assays for KRAS mutations and for aberrant NDRG4 and BMP3 methylation. The performance of the sDNA plus FIT panel was compared to the FIT results alone, by Receiver Operator Characteristic (ROC) analyses.

Results: 1047 individuals (51% male) with a median age of 60 years (range 50-75) were included, of which 7 (0.7%) had colorectal cancer and 104 (9.9%) had advanced precancerous lesions (advanced adenomas or sessile serrated polyps ≥1 cm).

The combination of sDNA and FIT was more sensitive than FIT alone for detecting advanced precancerous lesions (49% (50/102) and 25% (26/102), respectively). Specificities among individuals with non-advanced or negative findings (controls) were 89% and 96% for sDNA and FIT testing, respectively.

ROC analysis of CRC and advanced precancerous lesions compared to controls revealed an Area Under the Curve (AUC) of 0.75 for the sDNA plus FIT test, compared to 0.68 for FIT alone. At an equal specificity of 95%, advanced precancerous lesions were detected with higher sensitivity by the sDNA plus FIT test compared to FIT alone (36% vs 28%, p=0.08).

Conclusions: In an invitational colorectal cancer screening cohort, combining stool DNA markers with FIT detected more advanced neoplasia than FIT alone, primarily due to detecting more advanced adenomas.