PWE-104

IMAGE CYTOMETRY DNA PLOIDY ABNORMALITIES ARE AN INDEPENDENT RISK FACTOR FOR CANCER PROGRESSION IN NON-DYSPLASTIC BARRETT'S OESOPHAGUS AND LOW GRADE DYSPLASIA: RESULTS OF THE NIBR STUDY

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Introduction The risk of progression to oesophageal adenocarcinoma (OAC) from non-dysplastic Barrett's Oesophagus (BO) is low and unpredictable. Low grade dysplasia (LGD) may increase risk but is associated with significant interobserver variability by pathologists. Biomarkers are needed to better stratify patient risk. DNA ploidy abnormalities (aneuploidy/tetraploidy) reflect genomic instability and confer an increased risk of cancer progression, when measured by flow cytometry (FC). Image cytometry DNA ploidy analysis (ICDA) is a technique with equivalent accuracy to FC and uses formalin fixed tissue, allowing archival analysis.

Methods Multi centre nested case-control study conducted within the population-based Northern Ireland BO Register (NIBR), which includes all BO patients diagnosed between 1993 and 2005. Cases had histologically confirmed OAC or high grade dysplasia (HGD) diagnosed ≥ 6 months after BO diagnosis. Each case was matched to 3 BO controls, based on age (± 5 years), sex and year of BO diagnosis. Conditional logistic regression analysis was applied to investigate risk of progression prior to and post adjustment for potential confounders. Standard protocols for ICDA followed. All ICDA analysis was blinded to outcomes.

Results 89 cases of progression from BO to HGD/Cancer were matched to 291 BO controls. Of the 380 patients samples, 92% were successfully analysed by ICDA, including 78 cases. Mean ($\pm$ SD) follow-up time for cases and controls was 4.06 ± 2.95 years (range 0.5–12.1 years) and 7.42 ± 2.91 years respectively. There was a significantly increased risk for progression to OAC and HGD when DNA ploidy abnormalities were present (OR = 4.17; 95% CI = 2.37–7.35). After multi-variate analysis DNA ploidy abnormalities remained a significant predictor of risk for HGD and cancer (OR = 3.14; 95% CI = 1.64 to 5.98). In a risk model, the presence of DNA ploidy abnormalities and IND/LGD conferred a high risk of progression to OAC/HGD (OR = 52.93; 95% CI = 6.71 to 417.35). The risk of progression in patients who were diploid with IND/LGD or in patients with DNA ploidy abnormalities in NDBO was similar (OR = 2.23; 95% CI = 1.15 to 4.32).

Conclusion This multicentre blinded biomarker study demonstrates that DNA ploidy abnormalities measured by ICDA are independent risk factors for the development of OAC and HGD in BO. The presence of DNA ploidy abnormalities in patients with LGD confers a significantly increased risk of progression to OAC/HGD. This group may be suitable for endoscopic therapy.

Competing interests None.

Keywords aneuploidy, Barrett's oesophagus, biomarker, oesophageal adenocarcinoma.