ASSOCIATION OF HEALTHY AND UNHEALTHY PLANT-BASED DIETS WITH THE RISK OF COLORECTAL CANCER: OVERALL AND BY MOLECULAR SUBTYPES

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Background Several plant foods have been associated with a lower risk of colorectal cancer (CRC). However, not all plant foods are healthy, and little is known about the association between plant-based diets and specific molecular subtypes of CRC. We aimed to examine the association of healthy and unhealthy plant-based diets and the risk of CRC overall and by molecular subtypes.

Methods We followed 76,386 women in the Nurses’ Health Study (1984-2014) and 47,387 men in the Health Professionals Follow-up Study (1986-2014) for up to 30 years. Plant-based diets were assessed using two indices derived from the food frequency questionnaires: a healthy plant-based diet index (hPDI) and an unhealthy plant-based diet index (uPDI). Colorectal tumor tissues were collected to measure the status of microsatellite instability (MSI), CpG island methylator phenotype (CIMP), and BRAF and KRAS mutations.

Results During 3,143,205 person-years of follow-up, we documented 3077 incident CRC cases, including 1244 cases with MSI-high (MSI-H) and 1733 cases with MSI-low (MSI-L). A higher hPDI was associated with lower CRC incidence (hazard ratio [HR] comparing extreme quartiles=0.86, 95% CI: 0.77, 0.96; P-trend=0.04), whereas a higher uPDI was associated with higher CRC incidence (HR comparing extreme quartiles=1.16, 95% CI: 1.04, 1.29; P-trend=0.005). The association of hPDI significantly differed by KRAS status (P-heterogeneity=0.003) but not by other tumor markers. The hPDI was associated with lower incidence of KRAS-wildtype CRC (HR comparing extreme quartiles=0.74, 95% CI: 0.57, 0.96; P-trend=0.004) but not KRAS-mutant CRC (P-trend=0.22).

Conclusions A plant-based diet rich in whole grains, fruits, and vegetables was associated with a lower incidence of CRC, especially KRAS-wildtype CRC, whereas a plant-based diet emphasizing unhealthy plant foods such as refined grains might be associated with higher CRC incidence. These data emphasize the importance of differentiating healthy and unhealthy plant foods when promoting plant-based diets for the primary prevention of CRC. The differential association of hPDI by KRAS status suggests the interplay of diet and specific tumor pathways.