Associations between Post-treatment Inflammatory Biomarkers and Survival among Stage II-III Colorectal Cancer Patients

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We aimed to evaluate post-treatment inflammatory biomarkers, namely C-reactive protein (CRP), interleukin-6 (IL6), monocytes chemoattractant protein-1 (MCP1), leptin and adiponectin, in relation to overall survival (OS) in stage II-III colorectal cancer (CRC) patients. Methods: Participants were incident, invasive CRC cases who were 22–74 years of age, diagnosed between 1997–2008 from the population-based Seattle Colon Cancer Family Registry. We included stage II-III cases who were at the greatest risk for disease progression. Further restriction to 308 participants with a blood draw 1–3 years after diagnosis was made to preclude acute treatment effects. We measured concentrations of all five markers in EDTA-plasma samples using the Meso Scale Discovery immunoassays. Biomarker levels were log-transformed to ensure normality. We also divided patients into sex-specific quartiles for each marker to test for a dose-effect of a biomarker on disease progression. Mortality and cause of death were assessed through linkage to the National Death Index. We used Cox proportional hazard regression to estimate hazard ratios (HR) and 95% confidence intervals (CI) for associations of post-treatment inflammatory markers with OS. HRs were adjusted for potential confounders selected a priori, including age at blood draw, sex, body mass index, plasma storage time, the time between diagnosis and blood draw, and stage at diagnosis. Results: Elevated CRP levels were associated with poorer OS (HR = 1.32 per unit increase of log-CRP, 95% CI = 1.13–1.55). For circulating IL6, a dose-response relationship with survival was evident: compared with the lowest quartile of IL6, the 2nd, 3rd and 4th quartiles were significantly associated with OS, with HRs (95% CIs) of 2.72 (1.42–5.21), 4.23 (2.24–7.99), and 6.80 (3.56–12.96) respectively (p for trend < 0.0001). For MCP1, we observed a 2-fold increase in the risk of overall mortality per unit increase in log-MCP1 (HR = 2.17, 95% CI = 1.39–3.39). Circulating levels of leptin and adiponectin were not significantly associated with OS. Conclusions: Circulating inflammatory markers, specifically CRP, IL6, and MCP1, are prognostic markers in stage II/III CRC patients and should be considered for incorporation into studies of CRC outcomes.

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Oxylipins Correlate with Quality of Life in Women Taking Aromatase Inhibitors for Breast Cancer

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The purpose of this study was to determine if oxylipins – oxygenated bioactive lipid metabolites of ω-3 and ω-6 fatty acids with varying roles in inflammation and pain – correlate with aromatase inhibitor-associated arthralgia (AIA) and quality of life (QOL) in early stage breast cancer (ESBC) patients. Methods: ESBC patients on AI therapy were enrolled to an open-label study of sulindac, a non-steroidal anti-inflammatory drug (NSAID), for 12 months ($n = 47$). Pre-intervention arthralgia and physical function were assessed using the Western Ontario and McMaster Universities Osteoarthritis (WOMAC) questionnaire, where higher scores indicate worse symptoms. The Functional Assessment of Cancer Therapy – General (FACT-G) questionnaire was used to assess QOL, where higher scores indicate better QOL. A total of 53 plasma oxylipins in plasma were quantified by mass spectrometry. Pearson's correlation was used to measure the association between pre-intervention oxylipin concentrations, arthralgias and QOL. Results: Prior to initiating sulindac, baseline levels of 17 oxylipins were found to be significantly correlated with QOL scales. This included inverse associations between QOL and seven pro-inflammatory products of ω-6 fatty acid metabolism. Notably, prostaglandin E_2, the primary target of NSAIDs, was negatively correlated with Social Well-Being (rho = −0.30; $P = 0.04$). Conversely, resolvin D1, a potent anti-inflammatory lipid, was positively associated with Total FACT-G (rho = 0.31; $P = 0.03$) and Emotional Well-Being (rho = 0.37; $P = 0.01$). Two ω-3 metabolites with unknown mechanisms were correlated with both QOL and WOMAC; 19,20-DiHDPE was positively correlated with Total (rho = 0.34; $P = 0.02$) and Social FACT-G (rho = 0.32; $P = 0.03$), and inversely with Total WOMAC (rho = -0.303; $P = 0.04$) and Stiffness (rho = −0.32; $P = 0.03$); and 5 (6)-DiHETE was inversely correlated with Social FACT-G (rho = −0.33; $P = 0.02$) and positively with Total WOMAC (rho = 0.31; $P = 0.04$). Conclusions: This is the first evidence that plasma oxylipin metabolites of ω-3/ω-6 fatty acids correlate with QOL and arthralgia symptoms in patients on AIs and suggests oxylipins as a potential novel target for improving QOL and adherence to AI therapy in patients with ESBC.

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Accelerometer-measured Physical Activity and Breast Cancer Incidence in the WHI OPACH Study

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To examine the associations between accelerometer-measured physical activity (PA) and breast cancer incidence among a cohort of postmenopausal women. Methods: This longitudinal study included 6,382 women (mean age 79 ± 6 years; 49.4% non-Hispanic white, 33.7% non-Hispanic Black, 16.9% Hispanic) without a history of breast cancer who participated in the Women's Health Initiative (WHI) Objective Physical Activity and Cardiovascular Health (OPACH) Study. During 2012–2013, participants wore an ActiGraph GT3X+ accelerometer at the hip for up to 7 days. Accelerometer intensity counts were specially calibrated to PA in older women. The resulting data were used to compute minutes per day spent in total PA, light intensity PA (e.g., usual walking), and moderate-to-vigorous PA (MVPA; e.g., brisk walking). Physician-adjudicated first diagnosis of *in situ* ($n = 18$) or invasive ($n = 103$) breast cancer was ascertained over a median follow-up of 5.6 years. We used multivariable Cox regression to estimate covariate-adjusted hazard ratios (HRs) and 95% confidence intervals (CIs) for tertiles and one-standard deviation (SD) unit increments of PA exposures in association with breast cancer incidence. We examined effect measure modification by age, race/ethnicity, body mass index (BMI), and smoking history. Results: The highest (vs. lowest) tertile of total PA was associated with a breast cancer incidence HR of 0.67 (95% CI = 0.43–1.05) and this association was