



Western Surgical Association 2020 Annual Meeting

Monday, November 9, 2020
4:00pm – 6:15pm Pacific Time
– Virtual Meeting --

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1. AN ANALYSIS OF SEXUAL DIMORPHISM IN THE TUMOR MICROENVIRONMENT OF COLORECTAL CANCER

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Background: Women with colorectal cancer (CRC) have a survival advantage over men, yet the mechanisms underlying this are unclear. T-cell infiltration within the CRC tumor microenvironment (TME) correlates strongly with survival. We hypothesized that women with CRC have a different immune response than men, with increased T-cell infiltration and differential gene expression within the TME.

Methods: Tissue microarrays were created using primary tumor, tumor infiltrated lymph nodes, and uninvolved colon from 101 CRC patients. CD4-positive (CD4+) and CD8-positive (CD8+) cells were identified by immunohistochemistry and digitally counted. Genetic expression within the TME of primary and metastatic CRC tumors from 33 other patients was analyzed using the NanoStringIO360 panel. Immune and cancer related gene expression was quantified and compared between men and women.

Results: Patient age, tumor stage, and tumor location were not different between the sexes in either patient cohort. CD4+ cell counts were higher in women in the tumor (22.04% vs. 10.26%, $p = 0.002$) and lymph nodes (39.54% vs. 8.56%, $p = 0.001$). Interestingly, CD4+ was increased in tumor from women >55 years old vs. younger (40.2% vs. 23.4%, $p = 0.029$). There was no difference in survival of patients in the top CD4+ tertile compared to the bottom tertile. CD8+ infiltration was increased in uninvolved colon of women vs. men (47.4% vs. 34.6%, $p = 0.015$), and in tumor from stages I/II CRC versus III/IV (37% vs. 23.9%, $p = 0.009$). Increased survival was seen in patients in the top CD8+ tertile compared to the bottom tertile, likely due to co-association of higher CD8+ counts with lower stage (43.9 months vs. 25.3 months, $p = 0.007$). Differential genetic expression between men and women was noted, specifically regarding interferon signaling, immune cell adhesion/migration, and cytotoxicity pathways. In addition, expression was increased in women in genes related to T-cell signaling and chemotherapy response. Sexual dimorphism in gene expression was more pronounced in metastatic samples compared to primary tumor samples.

Conclusion: We demonstrate significant sexual dimorphism in the immune response to CRC that could contribute to the survival advantage seen in women. Investigation of the mechanisms behind this difference may reveal additional therapeutic targets.