DIFFERENCES IN HISTO-PATHOLOGICAL FEATURES OF COLO-RECTAL CARCINOMA BETWEEN DIABETICS AND NON-DIABETICS

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Background: Mechanisms postulated for increased cancer risk in diabetics include hyperglycemia, hyperinsulinemia, endothelial proliferation, and increased IGF-1 levels, receptor activation, and cytokine production. We plan to study the histopathological differences in the diabetic and non-diabetic colon cancer population.

Methods: Mechanisms postulated for increased cancer risk in diabetics include hyperglycemia, hyperinsulinemia, endothelial proliferation, and increased IGF-1 levels, receptor activation, and cytokine production. We plan to study the histopathological differences in the diabetic and non-diabetic colon cancer population.

Results: Univariately, diabetic patients had deeper tumor and lymphovascular invasion and higher TNM staging (OR and 95% CI: 2.06 [1.37, 3.10], 2.52 [1.74, 3.63], 2.45 [1.70, 3.52] respectively; p < 0.001 for all). After covariate adjustment, the effect of diabetes remained significant on those tumor characteristics (p < 0.005 for all). In multivariate analysis diabetics became significantly linked to presence of tumor components (log odds: 0.58 ± 0.25, p = 0.02) and were more likely to have signet ring cell carcinoma (log odds: 11.40 ± 5.28, p = 0.03). Age was negatively related to TNM staging (OR and 95% CI: 0.98 [0.96, 0.99], p = 0.003) and younger diabetic patients had signet ring cell carcinoma more frequently (p < 0.02). African American patients were less likely to be seen with deeper tumor invasion compared to White patients (OR and 95% CI: 0.51 [0.29, 0.88], p = 0.02). One year increase of age was associated with 3% lower risk of tumor lymphovascular invasion in diabetics against non-diabetics (p = 0.04). Proximal tumors were seen more frequently in diabetics, older patients, hyperlipidemics, and females (p < 0.05 for all). Hypertensives and hyperlipidemics were found to have a better level of tumor differentiation (p < 0.05).

Conclusion: Independently, the presence of lymphovascular invasion, higher staging, depth of invasion, proximal location, and a mucinous/signet/neuroendocrine component have all been associated with a worse prognosis in colorectal carcinoma. Our study found that each of these factors occurred in greater extent in colorectal cancer patients with diabetes. Signet-ring cell carcinoma is associated with a poor prognosis secondary to its increased tendency to invade and metastasize. This might be secondary to disruption of cell-cell adhesion by the E-cadherin/beta catenin complexes in these cells. Diabetics and younger patients were found to have this rare histology more often along with worst staging at presentation. Hyperinsulinemia and hyperglycemia can activate pathways stimulating proliferation, invasion, angiogenesis, and metastasis in colorectal carcinoma. Future research is needed to determine the role of 1) specific pathways for possible targeted therapies, 2) better glycemic control, and 3) aggressive adjuvant therapy. It may also be important to take an aggressive approach to diagnosis in younger population and an early institution of treatment. Our study found that hyperlipidemics and hypertensives had a better level of tumor differentiation. Previous studies have outlined a positive impact of hyperlipidemia on survival in colorectal carcinoma patients independent of the effect of other metabolic syndrome factors, including diabetes and hypertension. Further studies are needed to see the impact of hyperlipidemia, hypertension, and the interplay of metabolic syndrome factors on colorectal cancer histology to better explain these differences.