

ADVANCES IN ONCOLOGY

Current Developments in the Management of Solid Tumor Malignancies

Section Editor: Clifford A. Hudis, MD

Colorectal Cancer In Focus

The Impact of Glycemic Levels in Patients With Colon Cancer



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H&O How common is recurrence among patients with stage 3 colon cancer?

JM Approximately 150,000 people are diagnosed with colorectal cancer each year. About 25% of them are diagnosed with stage 3 disease, which indicates positive lymph nodes with no evidence of metastasis. Among these stage 3 patients, approximately 50% will be cured by surgery alone and 50% will recur. Adjuvant chemotherapy will improve the cure rate to approximately 70%, though it varies according to the number of positive nodes, the extent of bowel wall invasion, and other factors. The standard of care for adjuvant chemotherapy is a fluoropyrimidine plus oxaliplatin. Unfortunately, most of the patients who recur will eventually die from the disease.

H&O What have previous data suggested about diet in colon cancer survivors?

JM A few observational studies have previously looked at diet in colon cancer survivors. Most of the studies were small and included patients at different stages of colon cancer, including metastatic disease. In 2007, we published a study that examined patients with stage 3 colon cancer who followed a Western pattern diet, which is characterized by higher intake of red meats, processed meats, refined grains, and sugary desserts. Patients were classified as having higher or lower levels of a Western pattern diet. We found that patients with the high-

est level of a Western pattern diet had an approximate 3-fold increased risk in recurrence or death from colon cancer. All of the patients had undergone surgery and had received adjuvant therapy, so diet was an additional factor we considered after standard treatment. Those findings were the basis of our current study, in which we tried to tease out which factors within the diet, such as glycemic load, might impact outcome.

H&O What is glycemic load?

JM Glycemic load is an indicator of the body's response to food that can increase plasma glucose levels and, subsequently, insulin levels. Even in patients without diabetes, higher glycemic load can lead to higher overall basal insulin levels. We know that insulin and insulin-like growth factors can be growth factors for various cancer cells, including colorectal cancer. The thought is that patients who have either higher total carbohydrate levels or higher glycemic loads will have higher basal insulin levels at different times throughout the day, which can stimulate cancer growth.

H&O What was the design and outcome of your recent study examining glycemic load in colon cancer patients?

JM This prospective, observational study included patients with stage 3 colon cancer who had undergone surgery and were participating in the Cancer and Leukemia Group B

(CALGB) trial 89803, a randomized clinical trial comparing 2 chemotherapy regimens: fluorouracil and leucovorin versus irinotecan plus fluorouracil and leucovorin. Patients who participated in CALGB 89803 completed a semi-quantitative food frequency questionnaire approximately 2–3 months into their adjuvant therapy and then again at approximately 6–8 months after the completion of adjuvant therapy (or approximately 3–4 months and a year and a half after surgery). We used the results of both of these questionnaires to quantify various glycemic indexes, including glycemic load and total carbohydrate intake. We created quintiles of patients with higher and lower levels of glycemic load and examined disease-free survival, recurrence-free survival, and overall survival.

We found that patients in the highest quintile of dietary glycemic load experienced worsening in disease-free survival of approximately 80% compared to those in the lowest quintile. The difference was statistically significant. There were similar detriments in recurrence-free survival and overall survival. The findings regarding higher glycemic load were similar to those seen with higher levels of total carbohydrate intake.

We identified an apparent interaction with body mass index (BMI). Patients with a BMI greater than 25 kg/m², who are considered overweight or obese, seemed to be more affected by higher glycemic load than patients who had a BMI of less than 25 kg/m², who are considered normal weight or underweight. Glycemic load seemed to be a more significant factor in patients who were overweight or obese.

H&O Did anything about the study findings surprise you?

JM Our hypothesis was that glycemic load and total carbohydrates could impact outcome. The surprise was that

the association seemed to be stronger in patients who were overweight and obese. Glycemic load and total carbohydrate levels are both detrimental energy balance factors that can impact outcome in colon cancer. There is now increasing evidence that various energy balance factors could influence outcome in these patients. There appears to be a stronger detriment in patients who are overweight/obese and who have higher glycemic load levels.

H&O Can any recommendations be made to patients based on the results of your study?

JM This study was observational and not randomized, so it would be important to replicate and confirm in an independent data set. The findings are consistent with biological expectations. Although higher levels of glycemic load and total carbohydrates have been examined as risk factors for disease, this study is the first to examine whether these levels correspond to outcome in cancer patients. This study and the earlier one examining the Western pattern diet add to growing evidence that cancer survivors should consider a healthy, well-balanced diet with limitations in certain foods that might contribute to recurrence, particularly foods that can stimulate insulin levels.

Suggested Readings

Meyerhardt JA, Niedzwiecki D, Hollis D, et al. Association of dietary patterns with cancer recurrence and survival in patients with stage III colon cancer. *JAMA*. 2007;298:754-764.

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