A new study finds that patients with stage III colon cancer who follow the American Cancer Society’s (ACS) Nutrition and Physical Activity Guidelines for Cancer Survivors survive significantly longer than those who do not follow these recommendations \textit{[JAMA Oncol} [published online ahead of print April 12, 2018]. doi:10.1001/jamaoncol.2018.0126]. Specifically, the researchers found that faithfully following the ACS guidelines resulted in a 9% absolute reduction in the risk of death at 5 years.

“I believe the study is significant because it pulls together various factors that have been individually studied in colon cancer survivors to understand the association of more complete dietary and lifestyle behaviors on survival.” says lead study investigator Jeffrey A. Meyerhardt, MD, MPH, associate professor of medicine at Harvard Medical School and clinical director and senior physician at the Gastrointestinal Cancer Center at Dana-Farber Cancer Institute, both in Boston, Massachusetts.

The key recommendations of the ACS guidelines include:

- Achieve and maintain a healthy body weight and body mass index (BMI). If overweight or obese, limit the consumption of high-calorie foods and beverages and increase physical activity to promote weight loss.
- Engage in regular physical activity. Aim to exercise at least 150 minutes per week.
- Achieve a dietary pattern that is high in vegetables, fruits, and whole grains. Eat at least 2.5 cups of vegetables and fruits each day (≥5 servings/day). Choose whole grains instead of refined grain products. Limit the consumption of processed meat and red meat.

**KEY POINTS**

- Patients with stage III colon cancer who followed the ACS nutrition and physical activity guidelines survived significantly longer than those who did not.
- Clinicians should advise their patients with colon cancer about the role of diet, exercise, and lifestyle in improving survival outcomes.
- Eating whole grains plus eating 5 or more daily servings of fruits and vegetables appears to lead to improved colon cancer survival.
- Eating less red and processed meat did not appear to contribute to the benefit of the ACS guidelines.

**Study Design**

The prospective study included 992 patients with stage III colon cancer who were enrolled in the Cancer and Leukemia Group B adjuvant chemotherapy trial 89803 between 1999 and 2001. Patients were randomized within 8 weeks of undergoing surgical resection to receive 1 of 2 chemotherapy regimens, and they completed lifestyle surveys midway through chemotherapy and 6 months after they received chemotherapy.

For the survey’s dietary assessment section, patients completed a validated food frequency questionnaire that assessed their intake of 131 items over the prior 3 months. The patients reported whether they had...
ingested each of the items from never to 6 or more times per day. Items were classified as fruits, vegetables, whole grains, refined grains, red meat, processed meats, and alcohol.

For the physical activity assessment, patients indicated the average amount of time they engaged in 9 common physical activities over the previous 3 months for each activity, ranging from never to 11 or more hours per week. To calculate each subject’s total metabolic equivalent task (MET) hours per week of physical activity, the researchers assigned each activity a MET value, multiplied the activity-specific MET value by the amount of time the participant engaged in that activity, and summed across all activities.

Patients were assigned between 0 and 2 points based on their adherence to each of the main recommendations (BMI, diet, and physical activity), so that the overall ACS guideline score varied from 0 to 6, with a higher score indicating healthier behavior.

Study Results
Study participants ranged in age from 21 to 85 years (average age of 59.6 years), and less than one-half (43%) of the participants were women. On follow-up, the researchers counted 335 recurrences and 299 deaths, noting that 43 deaths were not related to recurrences.

When compared with patients with an ACS guidelines score of 0 to 1 (262 patients; 26%), patients with scores of 5 to 6 (91 patients; 9%) had a 42% lower risk of death during the study period (hazard ratio, 0.58; 95% confidence interval, 0.34–0.99 [P = .01 for trend]). The patients with higher scores also had a significantly improved disease-free survival (hazard ratio, 0.69; 95% confidence interval, 0.45–1.06 [P = .03 for trend]).

The researchers concluded that it is likely that following the ACS guidelines after a diagnosis of colon cancer inhibits recurrence and death. Specifically, achieving and maintaining a healthy body size, with physical activity and a healthy diet rich in vegetables, fruits, and whole grains as key facets leading to an appropriate BMI, improves insulin sensitivity, decreases inflammation, and increases vitamin D levels, which are biomarkers commonly associated with colorectal cancer survival.

The researchers concluded that each component of the score (BMI, physical activity, and diet) was independently associated with survival after colon cancer. However, they noted that the BMI range associated with the lowest risk of death for patients with colon cancer (23.0-29.9) was higher than the ACS guidelines’ recommendation (18.5-24.9). They wrote that “this may reflect reverse causation, since weight loss commonly occurs as cancer progresses. Alternatively, it is possible that a BMI of 23.0 to 29.9 reflects an optimal muscle mass-to-fat ratio for patients with colon cancer.”

For the physical activity component, the researchers found a benefit at 8.75 MET hours per week (approximately 150 minutes per week as recommended by the ACS) of moderate activity, including brisk walking.

For diet, eating whole grains instead of refined grains plus eating 5 or more daily servings of fruits and vegetables also led to significantly improved colon cancer survival. However, eating less red and processed meat did not appear to contribute to the benefit of the ACS guidelines, a result that confirms published findings from the ACS Cancer Prevention Study II Nutrition Cohort.

PERSPECTIVES: Research in Context

Marjorie Lynn McCullough, ScD, RD, senior scientific director of epidemiology research at the ACS in Atlanta, Georgia, says that the study provides an important contribution to the evidence base for guidelines for cancer survivors. “Much less is known about optimal diet and lifestyle after a cancer diagnosis compared to what is known about cancer prevention, which is why the ACS guidelines for cancer survivors also recommend following guidelines for cancer prevention.”

Dr. McCullough also notes that, “Because the colon cancer patients were participating in an adjuvant chemotherapy trial, the researchers had detailed clinical information on everyone in the study. In addition, all participants had been diagnosed with stage III colon cancer, so stage was not likely to confound the associations that they observed. Information on diet was available from 2 separate time points after diagnosis.” However, she also notes that this study did not collect information regarding usual diet before diagnosis, and therefore it remains uncertain whether the association of postdiagnosis diet is due to long-term dietary patterns before diagnosis or to post-diagnosis changes in diet.

Another strength of the study, Dr. McCullough says, is that although previous studies examined the individual guideline components and supported eating a healthy diet and...
being physically active after a colon cancer diagnosis, no previous study had examined the combined association of following all guidelines simultaneously with colon cancer outcomes. “Therefore, a key takeaway is that lifestyle may play an important role in prognosis after a colon cancer diagnosis.”

Dr. Meyerhardt says he believes a key takeaway from the study should be that there are additional factors beyond standard surgery and chemotherapy that may optimize outcomes for survivors of colon cancer. “Therefore, it is important for clinicians to discuss with patients the role of diet, exercise, and lifestyle.”

In their editorial (JAMA Oncol [published online ahead of print April 12, 2018]. doi:10.1001/jamaoncol.2018.0124) referring to this study, Michael J. Fisch, MD, MPH, Lorna H. McNeill, PhD, MPH, and Karen M. Basen-Engquist, PhD, MPH, emphasized its clinical importance but also questioned whether the conclusions can be generalized to patients with demographic characteristics not prominently represented in the Cancer and Leukemia Group B 89803 study. These would include adults aged younger than 50 years, those with an Eastern Cooperative Oncology Group/Zubrod performance status of 2 or lower, and nonwhite patients. They especially emphasized that African American individuals, who represented only 7% of the adjuvant trial cohort, have higher mortality from colorectal cancer. “Moreover, African American and Hispanic survivors are more likely to be obese and report poorer health status, and these factors affect physical function and the likelihood of meeting physical activity guidelines,” they write.

Dr. Meyerhardt says that the cohort for this study was derived from a population of patients with colon cancer who were treated at both community and academic practices. “I agree that confirmation of these results in subpopulations will confirm generalizability to all stage III colon cancer patients.”

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