Higher Levels of Physical Activity Significantly Increase Survival in Women With Colorectal Cancer

A recent analysis shows that women with colorectal cancer who engage in recreational physical activity before and after their diagnosis have significantly better survival (Cancer Causes Control. 2012;23:1939-1948). “We already have many good reasons to ask patients to exercise, but this article gives us another reason to emphasize being active, and staying active, after a diagnosis of colorectal cancer,” says corresponding author Amanda Phipps, PhD, staff scientist in the public health sciences division of the Fred Hutchinson Cancer Research Center in Seattle, Washington.

Using data from the Women's Health Initiative (WHI) study, the authors investigated the relationship between body mass index (BMI), recreational (both pre- and post-diagnosis) activity, and survival in postmenopausal women with colorectal cancer. The WHI is a study involving 161,808 women that was designed to investigate major causes of morbidity and mortality in postmenopausal women. Of these women, 1339 who developed colorectal cancer during the study were eligible for an analysis of associations between prediagnostic physical activity and BMI and survival. Altogether, 2093 women developed colorectal cancer, but exclusions included those with distant disease, a very low initial BMI, and a personal history of cancer (other than nonmelanoma skin cancer) prior to study enrollment.

At the time of enrollment, demographic data and medical and family history were obtained through self-administered questionnaires. A validated questionnaire that assessed recreational physical activity was completed by participants at baseline, as well as at 3-year and 6-year follow-up visits. Height and weight were measured at baseline, and were self-reported in subsequent years. “A unique aspect of this study is that the population is well characterized. We know a lot about the WHI participants over an extended period of time,” says Dr. Phipps.

Physical Activity Associated With Outcomes, Not BMI

The women were grouped into categories of physical activity: 0 metabolic equivalents (MET) hours/week, 0 or more to 2.9 MET hours/week, 3 to 8.9 MET hours/week, 9 to 17.9 MET hours/week, and 18 or more MET hours/week. A recreational activity level of 9 MET hours/week is equal to about 3 hours/week of moderate-intensity activity. Kaplan-Meier curves revealed significant differences between the groups with regard to all-cause mortality, but not in cancer-specific mortality.

In multivariate analysis, women with a prediagnostic physical activity level of 18 or more MET hours/week had a significantly lower colorectal cancer-specific mortality (32% reduction) and all-cause mortality (37% reduction) compared with women who reported no physical activity. The variables considered included patient age, tumor stage, ethnicity, education level, alcohol intake, smoking status, and use of hormone replacement therapy. The finding of lower mortality in the higher-activity group was more prominent among those with a normal BMI (with normal defined as 18.5 kg/m²-24.9 kg/m²). The group with an activity level of 9 to 17.9 MET hours/week had a decrease in colorectal cancer-specific (26% reduction) and all-cause (23% reduction) mortality compared with inactive women, but it was not statistically significant. No significant associations were found between BMI and mortality.

In all, 606 women were eligible for analysis of their postdiagnostic activity level (exclusions included those with missing data, those who received a diagnosis after...
the 6-year study follow-up interview, those who had died within 1 year of postdiagnostic measurement, or those who had a very low BMI (less than 18.5 kg/m$^2$). There was a statistically significant association between increasing levels of activity and lower cancer-specific and all-cause mortality. Women with a physical activity level of 18 or more MET hours/week had a 71% lower risk of colorectal cancer-specific mortality, and a 59% lower risk of all-cause mortality compared with inactive patients. Similar to the prediagnostic results, BMI was not associated with mortality. Dr. Phipps says the lack of an association between BMI and mortality is at least partially due to the fact that BMI measurements were taken at baseline when the participants entered the WHI, with a median time between baseline BMI measurement and colorectal cancer diagnosis of 5.8 years.

Furthermore, Jeffrey Meyerhardt, MD, MPH, gastrointestinal oncologist at the Dana-Farber Cancer Institute and associate professor of medicine at Harvard Medical School in Boston, Massachusetts added, “The investigators considered BMI $> 300$ mg/m$^2$ in their upper category. However, a prior study demonstrated that patients with BMI $> 35$ kg/m$^2$ experienced increased colorectal cancer recurrences and mortality. It may be that in colorectal cancer, higher levels of obesity are associated with outcomes” (J Natl Cancer Inst. 2006;98:1647-1654).

Several strengths cited by the authors include the study’s large sample size and prospective design, the fact that BMI measurements were taken by trained staff, and a comprehensive list of covariates was used in the analysis. Limitations include the lack of data on cancer treatment, self-reporting of activity as well as weight after the third year for some of the participants, the lack of follow-up BMI or physical activity measurements in some participants (thus possibly introducing selection bias in the postdiagnostic analysis), and the lack of a separate analysis of colon versus rectal cancer due to limited sample size.

“It is important to point out that this was an observational study. It is possible that the less active patients are just sicker overall, or that activity level is a marker of a healthy lifestyle that includes other factors that improve mortality rates,” says Dr. Phipps. A randomized controlled trial is currently underway from the National Cancer Institute of Canada that is evaluating the effects of regular supervised physical activity and behavioral support on disease-free survival after adjuvant therapy for patients with stage II or III colorectal cancer. The control group is given general information about nutrition and activity, but no supervised activity (Current Oncol. 2008;15:279-285).

**More Questions to Study**

Future studies to elucidate more specific details on the type and intensity of activity needed to improve outcomes, as well as how best to improve activity levels in patients, are needed. “We used MET hours/week as our activity measurement, but the same level of MET hours/week may include people who exercise at high intensity for a short period, and those who exercise at a low intensity over a long period,” says Dr. Phipps. Dr. Meyerhardt added, “Doing studies to test interactions with various molecular markers mentioned in the discussion of this paper is also important to better understand the biology behind the impact of physical activity and outcomes.”

Dr. Meyerhardt notes that there are still limited numbers of studies examining the impact of physical activity and obesity on outcomes in patients with colorectal cancer. “This paper is an important contribution to the growing literature that energy balance seems to impact outcomes of colorectal cancer survivors,” he says. “Ten years ago, there was minimal research on this topic and none in physical activity.”

**doi**: 10.3322/caac.21175