

Patients with advanced colon cancer having less surgery, better survival

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With the dawn of the modern era of new chemotherapeutic and biologic agents available for managing their disease, patients with metastatic colorectal cancer are undergoing less surgery for the removal of their primary tumors, according to research from The University of Texas MD Anderson Cancer Center.

The study, published in *JAMA Surgery*, also found an increase in overall survival in this patient population. Yet the researchers are left with questions about whether the rates of primary tumor resection (PTR) have not kept up with chemotherapy benefits and whether PTR rates should be even lower.

According to the American Cancer Society, more than 136,830 patients were diagnosed with colon or rectal cancers in 2014, and 51,260 died from the diseases. Of those newly diagnosed, 20 percent present with metastatic disease at the time of diagnosis, and in that population, 80-90 percent of the patients' tumors are unresectable.

The primary indication for PTR in metastatic colorectal cancer is for patients who develop symptoms such as obstruction and bleeding, explains George Chang, M.D., associate professor, Surgical Oncology and Health Services Research. In a select, but small group of patients, PTR should be performed in the context of treatment plans that include surgical resection of both primary and metastatic sites. However, many physicians and patients are concerned patients whose primary tumors are intact may develop such symptoms on chemotherapy, he explains.

"We know from a previous phase II, cooperative group study that it's safe to give chemotherapy even with biologics to patients with metastatic disease. Yet there's still controversy about the role of primary tumor resection because some believe that there's a survival association," says Chang, the study's corresponding author. "The purpose of our study was to evaluate the use of primary tumor resection among patients with metastatic colorectal cancer in everyday practice and nationally by examining trends in the proportion of metastatic patients undergoing PTR."

Chang and his team also wanted to examine the trends in survival outcomes among patients with advanced disease over the same time period to demonstrate that despite the decreased use of surgery, survival is improving.

For the retrospective, population-based study, Chang and his MD Anderson colleagues used the National Cancer Institute's (NCI) Surveillance, Epidemiology and End Results database to identify 64,157 patients, all of whom were diagnosed with metastatic colon cancer between 1988 and 2010. Overall, 43,273 (67.4 percent) underwent PTR, with those receiving the surgery more likely to be: female younger than 50 years old and married, and to have colon cancer and a high tumor grade.

The researchers found that the annual surgery rate decreased from 74.5 percent in 1988 to 57.4 percent in 2010, with the most dramatic annual changes in the rates of PTR occurring after 2001. Of note, says Chang, the more dramatic PTR changes correlate with the availability of new chemotherapy drugs.

Independent of receiving PTR, the researchers also found that the median relative survival rate of metastatic colon cancer patients improved from 8.6 percent in 1988 to 17.8 percent in 2009.

Regarding its limitations, Chang says the study doesn't directly compare survival among those who did and didn't get PTR, as the data available in SEER doesn't permit such evaluation without significant risk of bias. The researchers also didn't have information about the receipt of systemic chemotherapy, and while trends in rate of PTR and median relative survival were examined together, their study was not designed to establish a casual association.

"Our findings tell us that it is increasingly recognized that chemotherapy may be safely given to patients with tumors intact," he says. "Although fewer people are getting primary tumors resected, a large proportion of patients with metastatic disease at diagnosis are still having them removed. Together with the observation that primary tumor resection was more likely performed in younger patients who have colon rather than rectal cancers suggests that there may still be an overutilization of PTR and that careful consideration of the indication for such surgery should be made."

Chang hopes that the findings might help patients and physicians make decisions about the need for PTR in the metastatic setting, and that the potential benefit or harm of PTR in the absence of symptoms should be studied.

Chang and his colleagues are also presenting preliminary comparative data related to PTR and survival at the ASCO GI Meeting in San Francisco this week. He notes that a randomized study examining the issue is ongoing in Europe.

Beyond the current primary indication for PTR, ultimately, there may be a group of patients for whom it may be beneficial says Chang, because it may allow them to continue to receive chemotherapy. However, in the general population of metastatic colorectal cancer patients for whom resection cannot be performed, PTR may result in potential for

unanticipated delays or inability to receive systemic therapies that have shown to provide benefit.

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