

New study finds dramatic increase in metastatic colon cancer survival

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Novel chemotherapy and biological agents for metastatic colorectal cancer, combined with surgical advances in liver resection, have resulted in a dramatic increase in survival for patients with advanced disease, according to researchers at The University of Texas M. D. Anderson Cancer Center.

Published in the Journal of Clinical Oncology, it is the first study in the last 20 years to examine the survival rates for metastatic colorectal cancer, and finds that the median overall survival is now more than 30 months, compared to eight months for patients diagnosed before 1990. Five-year survival of patients diagnosed with the disease after 2004 is more than 30 percent.

Colorectal cancer is the fourth most common cancer diagnosed in the United States. According to the American Cancer Society, in 2008, more than 148,800 people were diagnosed and 49,960 died from the disease.

Recently, researchers have made great strides in identifying active agents for the disease, resulting in FDA approval of numerous chemotherapeutic agents, explained Scott Kopetz, M.D., assistant professor in M. D. Anderson's Department of Gastrointestinal Medical Oncology. Over the past decade, the concept that specific metastatic liver lesions can be surgically removed has become more widely accepted as practice. Thus, more emphasis is now placed on identifying candidates for resection of their liver metastasis.



"In this study, we wanted to determine if these changes resulted in longer survival of metastatic colorectal cancer patients in a large population base," said Kopetz, the study's corresponding author. "There had been some hints - for example, in Phase III trials we had seen the overall survival increase over several years. However, because of the enormity of the data, the large population data bases are slow to reflect these changes, so there had not been a signal of increased survival."

A second goal of the study was to determine which of the two modalities - surgery or chemotherapy - was responsible for the change in outcome, and when did the modalities have the most impact, explained Kopetz.

For the retrospective, population-based study, the researchers identified 2,470 newly diagnosed metastatic colorectal cancer patients at two institutions - M. D. Anderson (1,614 patients) and Mayo Clinic (856 patients) -- treated between 1990 and 2006. All patients received at least a portion of their therapy at one of the two institutions.

Of the 2,470 patients, 231 underwent hepatic resection, with the surgical procedure being preformed with increased frequency after 2000.

To determine the changes in outcome, the researchers looked to see if patients were able to undergo resection for their liver metastasis and when surgery outcome took place, as well as changes in chemotherapy utilization at the institutions over time.

The researchers found no significant change in overall survival in patients diagnosed 1990- 1997; the median for that date range was 14.2 months. However, during the time periods 1998-2000, 2001-2003 and 2004-2006, the median overall survival rates increased from 18 months, to 18.6 months, to 29.2 months respectively. Five-year overall survival also increased over time: from 9.1 percent (diagnosed 1990-1997); to 13 percent (diagnosed 1998-2000); to 19.2 percent (diagnosed 2001-2003).



Five-year survival for patients diagnosed 2004-2006 has not yet been determined but is projected to increase to more than 30 percent.

To confirm their findings, the researchers used the National Cancer Institute's Surveillance, Epidemiology and End Results (SEER), the population-based cancer registry, to identify 49,459 patients diagnosed with metastatic colon cancer between 1990 and 2005. The data showed early evidence of similar improvements in five-year and median overall survival in more recent years, said Kopetz.

"In the study, we found not only a significant improvement in overall survival for metastatic colorectal cancer patients, but we also demonstrated that the degree and rapidity of the improvement is of a magnitude that is rarely seen in metastatic cancers," said Kopetz. "Many of these patients are not necessarily disease-free, but living with their cancer with a high quality of life. For some patients, our goal of making metastatic colorectal cancer a chronic condition is closer to becoming a reality."

In the study, the researchers compare their findings to the incremental leaps of breast cancer survivorship of about a decade ago, when the development of new chemotherapy and hormonal agents revolutionized that disease.

Looking at when these changes in colon cancer survivorship occurred, the study showed two distinct time periods that reflect the impact of both hepatic resections and the availability of new novel therapies.

"Beginning in 1998 and even more by 2000, we started performing higher volumes of hepatic resections, and that coincides with the initial increase in survival. The second stage of improvement began around 2004, simultaneous to the approval of many more chemotherapy and biological agents - cetuximab, bevacizimab, oxaliplatin," said Kopetz.



"However, these two modalities are not independent phenomenon and certainly complement each other: as chemotherapy improves, we can remove more tumors, and as surgery for metastatic disease is more commonly performed, then patients can receive more chemotherapy."

Kopetz said the study emphasizes the need for more chemotherapy agents available in the fourth-line and beyond, as many metastatic colorectal cancer patients are outliving treatment options available to them. Also, despite the study's reported gains, metastatic <u>colorectal</u> <u>cancer</u> remains an incurable disease for the majority of patients and continued research is needed to further extended survival for patients, he said.

Source: University of Texas M. D. Anderson Cancer Center (<u>news</u> : <u>web</u>)

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