

CT imaging taken post avastin may predict survival in patients with metastatic colorectal cancer

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Using routine computed tomography (CT) imaging to analyze form and structural changes to colorectal liver metastasis after bevacizumab and chemotherapy may predict overall survival, according to research from The University of Texas M. D. Anderson Cancer Center.

The findings are published in the Dec. 2 issue of *JAMA*.

When combined with chemotherapy, the angiogenesis inhibitor bevacizumab, also known as Avastin, is associated with both improved survival in those with metastatic colorectal cancer and higher rates of pathologic response in patients undergoing surgical resection of colorectal liver metastases. The monoclonal antibody was approved for use in the front line setting of metastatic colorectal cancer in 2004.

However, the therapy presents a unique set of challenges, explains Jean-Nicolas Vauthey, M.D., professor in M. D. Anderson's Department of Surgical Oncology.

"We've known for years that tumor shrinkage is not necessarily a strong indicator of survival in this patient population, and this has been an area of much controversy and study within the cancer community," explained Vauthey, the study's corresponding author. "Some of these tumors are so aggressive and may immediately start to grow when a patient goes off bevacizumab-containing chemotherapy."

Prior to the *JAMA* study, Vauthey and his M. D. Anderson colleagues looked at pathology in patients who had undergone resection for colorectal liver metastasis, and found those who received bevacizumab in combination with chemotherapy achieved better pathologic response rates. Based on that pathologic finding of increased cell kill, Vauthey and colleagues then conducted a second preliminary study and uncovered that these patients were distributed in three groups - complete, major and minor response - with a strong survival correlation.

"Pathologic response has proven to predict improved survival and has been proposed as a new endpoint after surgery for colorectal metastases. However, a non-invasive method of predicting such a response to chemotherapy - especially biologic agents - does not exist," said Vauthey.

"Our preliminary findings correlated with observations made by our radiology colleagues and allowed us to hypothesize that we could move from pathologic criteria, which are postoperative in nature, to preoperative, radiological criteria, in evaluating a patient's response to bevacizumab. Our radiologists established a very simple imaging scheme of response. Using screening CTs to evaluate morphologic changes to the tumor, we selected criteria that stratified patients into one of three types of responses - optimal, incomplete or no morphologic response."

For the retrospective study, the M. D. Anderson researchers analyzed a total of 234 colorectal liver metastases from 50 surgical patients, all of whom underwent preoperative chemotherapy regimen that included Bevacizumab. Patients were treated at M. D. Anderson between 2004 and 2007; all underwent routine contrast-enhanced CTs prior to and following the neoadjuvant therapy. The median follow-up time was 18 months, with March 2008 being the last follow-up.

Blinded to pathologic results, treatment regimens and outcomes, Evelyne

M. Loyer, M.D., also a corresponding author, Chusilp Charnsangavej, M.D., Piyaporn Boonsirikamchai, M.D. all of the Department of Diagnostic Radiology, independently analyzed images for morphologic changes - from heterogenous masses with poorly-defined margins to lesions homogenous and cystic in nature with sharp borders - and then classified patients into one of the three groups.

"Our findings determined that the morphologic response was significantly associated with pathologic response, including the percentage of residual tumor cells," said Vauthey.

Optimal morphologic response corresponded with survival benefit after hepatic resection: the median overall survival for surgical patients who achieved optimal, complete morphologic response was not yet met. In those who had incomplete or no response, overall survival was 25 months.

To validate their findings, the team also analyzed a cohort of 82 unresectable metastatic colon cancer patients also treated with Bevacizumab-containing chemotherapy. In this group, optimal morphological response also correlated with survival, 31 months, compared with 19 months in those that achieved incomplete or no response.

From a radiological standpoint, Loyer said it's important to note that the morphologic criteria are a simple tool accessible to all radiologists involved with this patient population.

"The criteria were established with contrast enhanced CT using a routine technique available in all radiology practices without the need for any special equipment or software. Even more, the learning curve is short, the changes induced by the drug are striking and easy to recognize," she said.

Vauthey cautions that the study is both retrospective and preliminary, and needs to be validated in a much larger, prospective cohort. Still, he feels that these criteria have important implications - both medical and surgical.

"With these criteria, we now may be able to sit down with patients who receive chemotherapy containing anti-angiogenic agents - regardless if they will undergo surgery - and after just two or three months of treatment, have a meaningful discussion about their likely outcome," said Vauthey. "These findings also may have immediate surgical implications, as it might be possible in the future to propose more aggressive surgery in patients with more advanced disease, yet who are classified as having a major response, based on these radiological findings."

More information: *JAMA*. 2009;302[21]:2338-2344

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