

Study results define optimal waiting time before surgery following chemoradiotherapy

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Researchers analyzing data from the National Cancer Data Base (NCDB) have found that patients who had a cancer operation at precisely eight weeks—56 days—after the end of combined chemoradiotherapy had the best overall survival and successful removal of their residual tumors. The six-year study of almost 12,000 patients may bring clarity to doctors who have long debated the ideal waiting time between combined chemotherapy and radiation for rectal cancer and surgical removal of the cancer.

The study, published online in *Journal of the American College of Surgeons* in advance of print publication, investigated outcomes of 11,760 patients with advanced stage localized [rectal cancer](#) who had chemoradiotherapy and surgical treatment from 2006 to 2012. The patients had either stage II or III localized rectal cancer (stage IV is the most [advanced stage](#)). Christopher Mantyh, MD, FACS, of Duke University led the study, and its results were presented at the Southern Surgical Association meeting in Hot Springs, Virginia, in December 2015.

Colon and rectal cancers are the third most common cancers in the United States, according to the Centers for Disease Control and Prevention (CDC), with about 135,000 new cases and 51,000 deaths per year.* (*The CDC does not separate out colon and rectal cancers.*)

Dr. Mantyh noted that this study differs from previous studies that evaluated the interval between chemoradiotherapy and surgery for rectal

cancer in its sheer size; previous studies were typically smaller and involved single institutions. "Due to its size, we thought NCDB was a perfect resource to answer the question about the timing of surgery after chemoradiotherapy for rectal cancer. The data set represented all types of hospitals," Dr. Mantyh said.

NCDB, a joint program of the Commission on Cancer (COC) of the American College of Surgeons and the American Cancer Society, captures an estimated 70 percent of newly diagnosed cancer cases in the United States and Puerto Rico from approximately 1,500 cancer programs accredited by the CoC.

Patients with many types of cancer typically have a course of combined chemotherapy and radiation treatments before undergoing surgery to remove the tumors. The treatment before the operation helps to treat surrounding tissue and shrink the tumor. The researchers set out to determine the best timing interval in terms of two key measures of success in cancer treatment: margin positivity, that is, the cancer-free zone in the tissue surrounding the cancerous tumor after it is surgically removed; and tumor downstaging, which means the amount of the tumor that is downgraded in terms of its size and penetration into surrounding tissue. Secondary outcomes the study evaluated were readmission and death rates within 30 days of hospital discharge and overall survival.

The investigators found that the median time between chemoradiotherapy and surgery was 53 days, with the actual timing ranging from 43 to 63 days. "The odd thing about the study is that when we looked at the best timing for pathological downstaging as well as margin positivity, they both arrived at exactly the same time—56 days," Dr. Mantyh said.

The study analysis divided patients into two groups: short-interval, those who underwent operations within 55 days of chemoradiotherapy; and

long-interval, having had an operation 56 days or more after radiotherapy. The long-interval group was slightly older (age 59 vs. 58 years), more likely to be black (9.5% vs. 8%), treated at an academic hospital, and less likely to have private insurance (50.2% vs. 55.4%) and stage III disease (51.4% vs. 54.2%).

Moreover, extending the delay beyond 56 days between radiation and surgery did not result in a greater downstaging effect, but was associated with a higher likelihood of positive resection margins and compromised long-term survival, suggesting that longer waiting times may risk tumor regrowth. Long-interval patients also had a lower risk of returning to the hospital within 30 days after surgery with no difference in death rates in that period, but they also had worse long-term survival.

"The real significant thing we found was that long-term mortality was significantly higher after 56 days," Dr. Mantyh reported. Study results suggested longer wait times might risk tumor regrowth.

The study findings can bring some clarity to the debate among oncologists about the timing of an operation after patients complete radiotherapy. "In the global picture, there's a lot of discussion about if waiting longer for surgery is better, and if you don't wait as long there's less chance of tumor spreading, but none of it is backed up on good modeling data like we have in this study," Dr. Mantyh said. "This kind of analysis is what we need in medicine and surgery. We need to have good population based data."

More information: *Centers for Disease Control and Prevention. Colorectal Cancer Statistics. Available at: www.cdc.gov/cancer/colorectal/statistics/index.htm. Accessed January 6, 2016.

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