Medical Xpress

Investigating a better treatment sequence for esophageal cancer

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Looking for better ways to treat patients with esophageal cancer, University of Colorado Cancer Center member Martin McCarter, MD, is investigating whether a new treatment sequence will result in better outcomes.

As they await the results of a group of clinical trials—including one at the CU Cancer Center—McCarter and other University of Colorado researchers (led by surgery resident Bobby Torphy, MD, Ph.D.) looked

at data from the National Cancer Database to see if they could identify other patients who have undergone the new sequence, and what the outcomes for those patients were. The group published a paper in the *Annals of Surgical Oncology* in April detailing their findings.

We sat down with McCarter, professor of surgical oncology at the University of Colorado School of Medicine, to talk about the data and the next steps in his research.

Q: What is the motivation behind these esophageal cancer clinical trials and your review of the National Cancer Database data?

A: The big picture is that outcomes for esophageal cancer are still very poor, even in patients who can undergo an operation, and we're constantly looking for ways to improve that. The current standard of care is a combination of chemotherapy and radiation given together, followed by surgery. Treatment sequencing has evolved in other areas, particularly rectal cancer, in what is referred to as a "total neoadjuvant approach," in which patients get prolonged chemotherapy, followed by radiation therapy, then followed by surgery. They've been doing that in rectal cancer, and that has resulted in some improvements in cancer outcomes. The data for this approach in esophageal cancer is limited but in our minds it would make sense to try it. There are a couple of early-phase trials looking at that sequence, to see if it can help improve things for patients with esophageal cancer—including an investigator-initiated study here at CU led by CU Cancer Center member Jeffrey Olsen, MD. It's going to take a few years for those trials to mature, but in the meantime, we wanted to look at a large national database to see if we could determine if other people have been using this sequence. We used the National Cancer Database to ask that question, and we found about 5% of patients were getting this prolonged sequence. Based on the data, it appears that those patients actually have a better survival rate than patients who just get chemo and radiation prior to surgery.

Q: How does the sequence you're proposing differ from the current standard of care?

A: The current standard is that patients get five weeks of radiation, and they get a little bit of chemotherapy at the beginning and in the middle of that radiation therapy. Then they wait six or eight weeks, then they have surgery. This new approach adds chemotherapy for two to three months first, then transitions to chemo and radiation therapy, and then on to the surgery. The thought behind it is that in general, people don't die from the local cancer; they die from cancer that has spread microscopically before we even see it. If we treat them aggressively with chemotherapy first, then we are attacking the microscopic disease first and then following that by trying to control the local disease with radiation and ultimately with surgery as well.

Q: Is it easy to determine from the data if someone underwent this treatment sequence?

A: It is not. We had to make some assumptions and do some pretty significant modeling to answer the question. These determinations were based on dates within the database and the fact that the patients got pure chemo, followed by pure radiation, and then they got surgery. They had to have all three of those things, and then the dates had to be separated enough such that they weren't getting the standard chemo and radiation followed by surgery. The problem is we really don't know, just from the data, why they got chemo first. Maybe doctors were making some of the same assumptions we did, which is that we ought to hit them hard first, but they were doing that without a whole lot of guidance or trials.

Q: Could using this approach eliminate the need for surgery in esophageal cancer patients?

A: That's certainly the direction things have headed in rectal cancer.

People are a little less likely to avoid surgery in esophageal cancer just because the surveillance techniques are pretty inadequate. We know that a number of patients probably have a complete response to the chemo and radiation and may not need an operation; the problem is we can't really predict who those patients are, even with our best diagnostic scopes and scans.

Q: What's the next step in this research?

A: The next step is awaiting the formal results from the current trial. As a phase 2 trial, it's evaluating the potential toxicity of using this sequencing, but also evaluating the responses. Do we see better pathologic responses, and in the long term are there patients who don't need the esophageal surgery, or for those who do get the esophageal surgery, do we see improvements in overall long-term five-year survivorship? This data study was to set the table and see if we can learn any more about this sequencing strategy because we have very little to go on right now.

More information: Felix Ho et al, Induction Chemotherapy Plus Neoadjuvant Chemoradiation for Esophageal and Gastroesophageal Junction Adenocarcinoma, *Annals of Surgical Oncology* (2021). DOI: 10.1245/s10434-021-09999-5

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