Rectum-Preserving Watch-and-Wait Approach for Certain Patients Found Safe

BY ED SUSMAN

SAN FRANCISCO—A watch-and-wait approach that avoids radical surgery appears to benefit three out of four patients diagnosed with locally advanced rectal cancer if clinical signs of the disease disappear after chemo-radiation, according to data reported here at the Gastrointestinal Cancers Symposium.

The meeting is co-sponsored by the American Gastroenterological Association Institute, American Society of Clinical Oncology, American Society for Radiation Oncology, and Society of Surgical Oncology.

"From my experience, most patients are willing to accept some risk to defer rectal surgery in hope of avoiding major surgery and preserving rectal function," said Philip Paty, MD, Attending Surgeon in the Colorectal Surgery Service at Memorial Sloan Kettering Cancer Center, discussing his research in a presscast for reporters in advance of the meeting.

"We believe that our results will encourage more doctors to consider this watch and wait approach in patients with clinical complete response as an alternative to immediate rectal surgery, at least for some patients," he said. "Non-operative management appears to be a safe and effective treatment strategy and achieves a high rate of rectal preservation."

Retrospective Review

In the retrospective review, he and his colleagues compared the outcomes of 73 patients who deferred surgery after chemoradiation therapy with those of 72 others who did undergo surgery to eliminate cancer in the rectum. After 3.5 years of follow-up, 54 (74%) of the patients in the non-operative management strategy group had a durable, sustained clinical complete response without clinical intervention on the rectum, and the longest follow-up in this group of patients is more than eight years.

"On the other hand, 19 patients—or 26 percent of the group—did experience local regrowth of tumor," Paty said. Sixteen of these regrowths were within the wall or the rectum. These are growths that can be detected with endoscopy or physical exam of the rectum. Three patients had regrowth in the lymph nodes around the rectum which requires imaging for detection.

"All 19 patients were able to have surgical salvage, and in all cases the operation was successful —all of the tumor was removed with clear margins," he said. "In 17 cases that was a full rectal resection; and in two cases with small tumors, the surgeon was able to perform local excision.

"We observed a 98 percent rate of local control in combination with salvage surgery. One person had cancer recurrence after surgery for a re-growth. So with the 54 patients who have not required any surgical intervention and the two patients with local excision, there are a total of 56 patients or 77 percent of the total who have had their rectal function preserved."

The 72 patients, who had surgery upfront, did not have rectal preservation, but none of those patients experienced recurrence. These patients either had rectal reconnection surgery or had a permanent colostomy, he said.

Regarding disease-specific survival, there were four deaths among those who opted for non-operative management and there were two deaths among patients who had rectal resection. "This was not statistically significant (P=0.3374)," Paty said. In overall survival—death due to any cause, there were six cases in the non-operative management group and four in the group who underwent surgery (P=0.4713).

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Improved Quality of Life

The moderator of the news conference, Smitha Krishnamurthi, MD, Associate Professor of Hematology and Oncology at Case Western Reserve University School of Medicine, said: "These are important findings for patients with rectal cancer because removal of the rectum can result in altered bowel habits or the need for colostomy.

"In this setting, non-operative management compares favorably with resection. We do need longer follow-up, though, to be sure that these patients have disease-specific survival that equals what is achieved with surgery over the long term."

Paty noted that locally advance rectal cancer is the most common presentation of the disease, meaning that the cancer has extended through the muscular wall (Stage T3 or Stage T4) or has spread to the regional mesenteric lymph nodes (N1 or N2 disease)—"This is generally based on pre-surgical evaluation."

3 Components of Standard Management in U.S.

The standard management for more than 10 years in the United States has been to treat with three components of therapy, he explained: Neoadjuvant chemoradiation to the pelvis; rectal resection; and in most patients, adjuvant chemotherapy.

But studies have shown that from 12 to 38 percent of patients will have no cancer cells in the resected specimen, and "this raises the question of whether

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surgery is always necessary in the subset of patients when the response is very favorable."

"Since 2006, with mutual consent of the patients and the surgeon, non-operative management for patients with a clinical complete response has been used selectively—not routinely—at our institutions," he said. "These are the patients we are evaluating in this study."

During that period, 442 patients from 2006 to 2013 were treated for locally advanced rectal cancer and underwent neoadjuvant chemoradiation. One group of 73 patients who had a clinical complete response were treated with non-operative management. In these patients doctors were unable to detect cancer on physical exam, endoscopy, or imaging.

"For comparison we retrospectively identified 72 patients who also had neoadjuvant therapy and underwent surgery and were found after surgery to have no cancer cells in the specimen," he said. "They represent a very high bar for comparison."

> "Prospective trials to confirm these findings are in progress."

Paty said the researchers sought to assess the safety and efficacy of non-operative management: "We wanted to see the efficacy of this approach—meaning how often is rectal preservation successful in the non-operative management, and the biologic safety component was to see how non-operative management compared with radical resection among patients with no residual cancer cells."

By avoiding rectal surgery, patients are spared its risks, including impaired bowel and sexual function, which can substantially diminish quality of life, he said.

"A quality-of-life analysis is being conducted," he noted. "We collect quality-of-life data prospectively on all our patients, and we will compare our non-operative management patients with those patients who have had a resection and, ideally, with normal controls."

"Patients who have undergone resection often come in with bleeding, pain, and need for frequent evacuation. It's pretty obvious that if you can avoid rectal surgery, quality of life is far superior to those who have had rectal resection."

Rigorous Surveillance

Patients who opt for non-operative management undergo a rigorous surveillance regimen, Paty said. "The surveillance is time dependent. The role of surveillance is usually shared by the surgeon and the medical oncologist, and sometimes a gastroenterologist. From the surgeon's point of view, the goal is to survey the patient for local regrowth. Our data and other data suggest that is a salvageable condition. We know the risk is greatest in the first 18 months after chemoradiation.

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"For that first year to year and a half, I have patients in every three months for flexible sigmoidoscopy and digital exam and general imaging every six months. Over time that interval widens for examinations. Generally in the second and third years it is every four months, and then every six months out to five years, and yearly after that.

One of Largest Studies of Its Kind

According to the authors, this is one of the largest experiences of its kind, building on prior evidence from research conducted in Brazil and the Netherlands. "Prospective trials to confirm these findings are in progress," Paty said.

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