

Rectal Cancer Trial Supports Preoperative Radiation

BY TIMOTHY F. KIRN
Sacramento Bureau

SEATTLE — Rectal cancer patients who got radiotherapy before their surgery had a lower local recurrence rate—even in T1 and T2 stage tumors—than did those who did not receive prior radiotherapy, according to preliminary results of a British trial.

“Meticulous surgery producing clear margins in patients with favorable tumors is simply not enough,” Dr. John R.T. Monson said at the annual meeting of the American Society of Colon and Rectal Surgeons.

The prospective Medical Research Council CRO7 trial enrolled 1,350 patients with adeno-

carcinoma of the rectum, in 80 centers, 69 of which were in the United Kingdom. Patients were enrolled between 1998 and 2005, said Dr. Monson, a professor in the academic surgical unit at the University of Hull and Castle Hill Hospital, Cottingham, England.

A total of 674 patients were randomized to receive radiation treatment before surgery (25 Gy), and the remaining 676 received radiation treatment after surgery (45 Gy) if they had a positive margin in their resection. All of the patients received postoperative chemotherapy, according to accepted protocol, on the basis of their lymph node status. About two-thirds of the patients had a low anterior resection, and one-

third had an abdomino-perineal excision.

The investigators found that after a median follow-up of 3.5 years, local recurrence was 5% in the 674 patients who received presurgical radiotherapy, compared with 11% in the 676 subjects who did not. And when the cancers were broken down by T category and analyzed by margin status, the investigators found that for every individual stage, the local recurrence rate was lower with radiation therapy given before surgery. (See chart.)

To date, the local recurrence rate in patients who had a clear circumferential resection margin and received prior radiation is 4%, vs. 14% in the group that didn't receive prior radiotherapy. For those with a positive margin, the rates are 16% and 31%, respectively.

Disease-free survival, a secondary end point in the trial, also was significantly better at 3 years: 80% in the prior-radiotherapy group vs. 75% in

the group that didn't receive prior radiation. At 5 years, disease-free survival was 75% vs. 67%, but this difference was not statistically significant—a fact that Dr. Monson attributed to the small

At 3 years, disease-free survival was significantly better (80%) in the prior-radiation group than it was in the non-prior radiation group (75%).

number of patients (138) who reached 5 years post surgery.

“These are relatively early data, and we suspect that if the curves continue to move in this direction, they will be significantly different in due course,” Dr. Monson said.

Despite the varied locations, the quality of the trial—the surgery in particular—appeared to be good and is not likely to become an issue, Dr. Monson said.

Positive margins were found in about 10% of both groups. However, the rate of positive margins declined consistently over the course of the trial. This indicates that as the surgeons be-

came more experienced, they improved, which suggests that their competence generally was good, Dr. Monson asserted. “The quality of the surgery in this trial was high,” he said.

The most common surgical complication in the anterior resection group was anastomotic dehiscence, occurring in 8% of the prior-radiation patients and 7% of the patients who didn't receive prior radiotherapy. The most common complication in the abdomino-perineal excision group was a nonhealing perineum, occurring in 36% and 22% of the patients, respectively.

The biological factor that appeared to be of most relevance to local recurrence was extramural vascular invasion. The study found that when patients had extramural vascular invasion, they were four times as likely to have a local recurrence.

“We believe this is likely to be one of the potential explanations for the incidence of local recurrence occurring in those patients with the most favorable tumors,” Dr. Monson said. ■

Local Recurrence of Rectal Cancer by Tumor Staging

Stage	Recurrence Rate With Prior Radiation	Recurrence Rate Without Prior Radiation
I	0%	6%
II	2%	12%
III	10%	25%

Note: Based on a median follow-up on 674 patients in a period of 3.5 years.
Source: Dr. Monson

ELSEVIER GLOBAL MEDICAL NEWS

Lab Test Combo Helps Tease Out Pediatric Appendicitis Diagnosis

BY ROBERT FINN
San Francisco Bureau

SAN FRANCISCO — The diagnosis of appendicitis is notoriously difficult in children, with estimates of misdiagnosis rates ranging from 28%-57% for children over the age of 12 and up to 100% for children under 2 years of age.

But the diagnosis may be made with high specificity using a combination of C-reactive protein and white blood cell levels, suggest the findings of a poster presented by Dr. Karen Y. Kwan and Dr. Alan L. Nager at the annual meeting of the Pediatric Academic Societies.

In particular, a C-reactive protein (CRP) level of 1.0 mg/dL or greater combined with a WBC count of 15,000 cells/mm³ or greater yields a specificity of 90%, a sensitivity of 49%, a positive predictive value of 86%, and a negative predictive value of 59% for confirmed appendicitis.

The study, conducted at the University of Southern California, Los Angeles, involved 209 patients aged 1-18 years presenting at a tertiary urban children's hospital with abdominal pain suspicious for acute appendicitis.

In addition to history, physical exam, x-ray studies, and histopathology, the investigators conducted blood tests for CRP, WBC, D-lactate, and procalcitonin.

Two to 6 weeks following discharge from the emergency department, investigators followed

up with the patients to determine the ultimate diagnosis.

Of the 209 patients, 115 (55%) had confirmed appendicitis and 94 (45%) were negative for appendicitis. Among the diagnoses for children negative for appendicitis were constipation, gastroenteritis, pyelonephritis, ovarian torsion, and neoplasm.

The mean D-lactate values did not differ between patients who were positive and negative for appendicitis. The values of the other three lab markers did differ significantly; in each case patients with appendicitis had a significantly higher level than patients without.

Using a cutoff value of 1.0 mg/dL of CRP alone would yield a sensitivity of 84% and a specificity of 70%. A combination of that CRP cutoff with a WBC cutoff greater than 15,000 cells/mm³ results in a slightly lower sensitivity, a specificity of 90%, and the positive predictive value of 86%.

The investigators noted that there are several reasons to interpret their findings with caution. First, 85% of the patients were Hispanic, and they came from a largely indigent population. In addition, one cannot exclude the possibility that acute or chronic diseases may skew the laboratory values.

The meeting was sponsored by the American Pediatric Society, the Society for Pediatric Research, the Ambulatory Pediatric Association, and the American Academy of Pediatrics. ■

Suspect Perforated Appendix If Bilirubin Level Is High

LOS ANGELES — Elevated serum bilirubin on admission may be a tip-off to a perforated appendix, according to research from the University of Southern California, Los Angeles, that was presented at the annual Digestive Disease Week.

Dr. Joaquin Estrada and his associates in the department of surgery at the university reported that those patients who had a gangrenous and/or perforated appendix were 2.9 times more likely than were other patients with suspected appendicitis to have a total bilirubin greater than 1 mg/dL upon admission.

The team retrospectively reviewed the charts of 41 patients who were found to have a gangrenous/perforated appendix at surgery.

Dr. Estrada and his colleagues also looked at a total of 116 patients who had been admitted for suspected acute appendicitis but who were not found to have a perforated or gangrenous appendix.

A pathologically normal appendix was found in 13 of the

patients in the latter group.

Among those patients with perforation, a total of 23, or 56%, were found to have had an elevated bilirubin upon admission compared with 36, or 31% of those who were not found to have a perforated or gangrenous appendix.

There were several factors that did not distinguish the two groups. These factors included the duration of symptoms, the total white blood count, elevated temperature, systemic inflammatory response score, and patient age.

While larger studies are needed, Dr. Estrada said that these findings may help to assist clinicians “in determining which patients you'd like to get a CT scan on.”

A potential mechanism for raising bilirubin, based on animal studies, is a biochemical response to bacteremia, Dr. Estrada said.

Patients were not included in the 12-month review of cases if they had liver disease, alcoholism, hemolytic disorders, or biliary disease.

—Betsy Bates