

RECTAL CANCER IN THE ELDERLY

By: Gil Lederman, M.D.

There are always issues in medical care and specifically in oncology about what is appropriate treatment for the older patient. Many physicians make judgments about what an older person might be able to tolerate. There are issues of surgery, anesthesia as well as tolerance to chemotherapy and radiation.

Each physician has experience that is one's own. There are also in some instances guidelines. Furthermore, some older patients are aggressive about seeking medical care while others are passive or negative. Similarly the same is true with families. Some push for every measure despite hope while others are eager to offer no treatment. There is research, however, being done for care of elderly patients in the field of oncology and elsewhere. Care of older citizens is important as an increasing number of us are going to be in older age group. Some might find us old as we are. It is estimated that within 30 years 20% of Americans will be over 65 years of age. This is important in oncology since the majority of cancer patients are over 65 and more than half of these are older than 70 and one-fourth greater than 80 years of age. In some studies older patients are excluded by age criteria and otherwise by co-morbid disease.

Studies have showed that older people tend to receive chemotherapy and radiation less often. Thus, many older patients do not receive what is considered the standard of care.

For patients with colon cancer, post-surgical treatment is dependent on the stage or extent of the cancer. If lymph nodes contain cancer then chemotherapy is generally administered. The usual drugs are Fluorouracil and Levamisole. These drugs reduce death rate by approximately a third compared to surgery alone.

In general, these drugs are used for about half a year after surgery for colon cancer containing lymph nodes. Some patients receive these drugs even when lymph nodes are not involved in an attempt to enhance survival.

Historical evaluation of patients in this country have shown that ten years ago only 48% of patients 65 to 74 years of age received the recommended therapy and only 24% of those aged 80 to 84 received adjuvant therapy known to enhance survival. The paradox is, of course, that patients in their 70's have a life expectancy without cancer of at least a decade. Thus, with this projected survival and known benefit it is reasonable to evaluate the role of chemotherapy in elderly patients.

A group of researchers led by Sargent et al in a multi-institutional study designed a study to evaluate treatment in elderly with colon cancer. Seven studies were found that met criteria to be evaluated as part of a pooled database. In these studies, patients were randomly allocated to receive no treatment or chemotherapy after surgery. Other studies used Fluorouracil and Leucovorin, while two used Fluorouracil and Levamisole.

Patients had advanced adenocarcinoma of the colon with treatment beginning 21 to 56 days after surgery. Treatment of Levamisole and Fluorouracil was one year while Fluorouracil and Leucovorin was six cycles in four of the studies and twelve cycles in the fifth analysis.

In the seven studies there were 3,437 patients, 2.5 of these patients were ineligible leaving 3,351 patients. Fourteen hundred and forty six or 43% had Stage II disease and one thousand nine hundred and five had Stage III disease.

For patients 50 years old or younger there was a 2% chance of death without detectable cancer. In patients 70 years of age or older there is a 13% chance of death without cancer.

Nearly a third of the deaths among older patients were due to causes other than cancer. Five percent of the youngest patients died from causes other than cancer. It should be noted that 30% of patients in both groups died with recurrence of cancer over 8 years.

The studies showed beneficial results of chemotherapy in terms of survival time to recurrence. There was statistical analysis performed to show this was indeed meaningful. Five-year survival was 71% in patients who received chemotherapy. It was 64% in untreated patients after surgery. Five-year cancer free survival was 69% in people who received chemotherapy compared to 58% in people who do not receive chemotherapy.

The researchers looked at survival and cancer-free life and compared to adjuvant chemotherapy with no adjuvant chemotherapy by age group and found them to be similar for the five years after treatment.

People who received Fluorouracil and Levamisole had more lowering of blood count, nausea and vomiting than those who had Fluorouracil and Leucovorin. However, the people who have Fluorouracil and Leucovorin had more stomatitis or inflammation of the mouth and diarrhea than the other group. Age did not enter in as a factor with higher rates of nausea, vomiting, stomatitis or diarrhea in either chemotherapy arm. There was worse lowering of the white blood counts in older patients who received Fluorouracil and Levamisole as a relationship of age.

The people who received Fluorouracil and Leucovorin or Levamisole had a 7% absolute increase in 5-year survival. In a 5 year cancer free survival 69% compared to 59% in untreated patients. There appeared to be no difference in susceptibility of colon cancer to chemotherapy in younger and older patients.

The researchers concluded, "The principle limitation of this study concerns its potential applicability to the general population of elderly patients. As a result of exclusion criteria and screening, elderly patients who enter clinical trials are a select group, with good performance status in cognition, access to transportation, and limited numbers of co-existing conditions. Although many elderly patients in the community have similar characteristics, others have multiple co-existing conditions, malnutrition, and poor social support. How these factors might affect the efficacy and tolerability of Fluorouracil base chemotherapy is unknown. Until further studies are performed, the decision to treat an elderly patient who has several other problems should include the physicians, patient and family.

Only 23 of the 3,351 (0.7%) in the trials were analyzed were over the age of 80 years. Caution is therefore advised in extrapolating these findings to octogenarians. However, in the sub-group of octogenarians who are robust enough to meet typical protocol eligibility requirements, the data offers no clear contraindications to the therapy and supports the assertion that treatment should be considered for selected persons among even the oldest patients with colon cancer. In addition, the data supports the notion that these patients should be considered appropriate candidates for clinical trials of chemotherapy."

"In this study, as expected, the oldest patients had a higher probability of dying without evidence of recurrence (13%) than the youngest patients (2%). In addition, 32% of the deaths among the oldest patients, but only 5% of the deaths among youngest patients were due to causes other than cancer. Nevertheless, most deaths in all age groups were due to colon cancer. Thus, it is reasonable to consider chemotherapy nearly all patients with resected Stage II and Stage III colon cancer."

An editorial by Muss, from the University of Vermont reported that, "Clinical trials remain the cornerstone of therapeutic advances in oncology. Historically older patients were excluded from any clinical trials. Although age restrictions now have been abandoned, the representation of older patients in clinical trials is still woefully inadequate. Of 16,396 patients consecutively

enrolled in 164 treatment trials conducted by the South West Oncology Group between 1993 and 1996, only 25% were 65 years or older, although census data indicated that at least 63% of the population with cancer being studied were in this age group.

Another study found that only 35% of women with cancer who were over 65 were offered participation in clinical trials, as compared with 51% of those who were younger. After adjustment for co-morbidity, stage of cancer, race, and functional status, older age remained a statistically significant predictor of not being asked to participate in a trial. When they were asked to participate, 56% of younger patients and 50% of older patients consented. Major barriers to participation in the clinical trials for older patients include aggressive therapies with substantial toxicity, the larger number of co-existing illnesses, the small number of trials designed for older patients, the patients' limited expectations of long-term benefits, and lack of financial, logistic and social support.

What can be done to overcome the bias against offering potentially beneficial chemotherapy to older patients? First, leaders in the fields of gerontology and oncology must educate physicians and the public about the appropriate use of chemotherapy in older patients.

Second, more researchers needed to know the effects of co-morbidity on tolerance and outcomes of treatment. The National Cancer Institute and the National Institute on Aging have provided funding initiatives for the much-needed research in this area.

Third, appropriate financial and social support for clinical trials in older patients must be provided. The centers for Medicare and Medicaid services now pay for non-research related medical costs for patients enrolled in clinical trials. Age alone should not be used to deny potentially beneficial treatment to any patient with cancer."

Appropriate treatment of rectal cancer can improve survival and decrease cancer recurrence. We have innovative programs at Radiosurgery New York to treat recurrent or metastatic rectal cancer in the pelvis, abdomen, and liver or beyond using fractionated stereotactic radiosurgery. Those with rectal cancer may wish to contact our experts at 212-CHOICES or e-mail questions to gil.lederman@rsny.org. We also have multidisciplinary panel of experts to review each patient's case. Additionally we also have seminars open to the public on a regular basis.