

SEARCHING FOR BEST TREATMENT OF GASTROESOPHAGEAL JUNCTION CANCERS

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The gastrointestinal tract extends from the mouth through the throat, esophagus and into the stomach and its first or a proximal areas. A particular type of cancer that occurs at the junction between the esophagus and the stomach is called gastroesophageal carcinoma. A variety of treatments are available for cancers there including surgery, radiation and chemotherapy.

Recently a study published by McDonald in the prestigious New England Journal of Medicine was published. The purpose of the study was to evaluate surgery alone versus surgery followed by chemotherapy and radiation in order to find the best results. Best results means greater survival and the least side-effects. Most believe that randomized studies - when properly designed - offer the best information about treatment options. Randomized studies offer different treatment options that are chosen by random computer design without patient or physician bias. The only decision by a patient is that one is to participate in it.

Unfortunately most patients who go through surgery are not cured. In fact even for patients with the earliest cancers stage IA, which are those limited to the gastric mucosa, the ten-year survival rate is 65%. For those having more advanced cancers the survival rate can fall to as low as 3%. It's easy to see why improvement is needed. There is an obvious need for better results.

Because of the high recurrence rates observed after surgery, many recommend chemotherapy and radiation. This is considered routine in many corners of the medical community.

A particularly common site of cancer recurrence is in the area where the cancer first began. It is estimated that local or regional recurrence for gastric cancers can be as high as 65% even after surgery. Local or regional recurrence means the cancer comes back to the resected area despite surgery. Many fail to understand the biologic principles of cancer growth after surgery.

Because local recurrences are so high it would suggest that cancer cells have been left behind and that local or regional radiation is an appealing method to consider. A group of researchers nationally put together a study to evaluate the potential benefits of chemotherapy and radiation combined after surgery versus surgery alone for those with cancer of the stomach or gastrointestinal junction.

Patients were eligible for this study entitled Searching For Best Treatment of Gastroesophageal Junction, if there was an adenocarcinoma of the stomach or gastrointestinal or GE junction. There needed to be a complete removal of the cancer with resection of all the cancer including those at the margin.

Patients were then staged. The staging system is a method to determine the extent of the cancer. Usually this includes endoscopy, CT scanning with contrast, blood tests and physical examination. If symptoms dictate, other tests such as a brain MRI scan, x-rays and bone scans are performed.

Patients, after removal of their stomach cancers were randomly allocated to have that surgery alone or to receive chemotherapy consisting of Flurouracil and Leucovorin combined with local or regional radiation. The randomization process took place within forty days after surgery.

The dose of Flurouracil was 425mg/m² per day and Leucovorin 20mg/M² per day for five consecutive days. This chemotherapy dose is given in milligrams per meter squared of body surface area. The chemotherapy/radiation started on day 28 after the initial cycle. The dose of radiation was 4500 cGy at 180 cGy or centigrade per day. Centigrade (or cGy) is a measurement

of radiation dose. The radiation was given over twenty-five treatments in five weeks to the tumor bed, regional lymph nodes and 2cms beyond the margins of removal of the cancer. After the completion of the radiation, two further cycles of Flurouracil and Leucovorin were administered. If there were side effects from the chemotherapy the dose was diminished.

Between 1991 and 1998, six hundred and three patients were registered on this study but forty-seven or 8% were ineligible because of positive surgical margins or other disease. Thus five hundred and fifty six patients remained with two hundred and seventy five allocation to surgery only and two hundred and eighty one to surgery plus chemotherapy/radiation.

Most tumors were felt to be in the distal stomach but the GE junction comprised 20% of cancers. Two thirds of the patients had T3 or T4 tumors and 85% had cancer in the lymph nodes. The T3 or T4 stages refer to the extent of the primary cancer.

There were side effects of treatment including the lowering of blood count and gastrointestinal effects. Some had nausea, vomiting or diarrhea.

The median follow-up time of patients was five years and the survival was thirty-six months, median, in the chemotherapy/radiation group yet only twenty-seven months in the patients receiving surgery alone. At three years 50% of the chemotherapy/radiation patients were alive compared to 41% in the surgery only group. Statistical analysis was performed to show that the benefit to receiving chemotherapy and radiation was real.

The time to relapse was thirty months and the chemotherapy/radiation relapses compared to nineteen months in the surgical only relapses. The majority of patients having surgery alone relapsed (64%), while the minority of chemotherapy/radiation patients relapsed (43%). Local and regional relapse occurred in 29% of the surgical only group but only 19% of the chemotherapy/radiation group. Regional recurrence occurred in 72% of those relapsing in the surgical group and 65% of those in the chemotherapy/radiation group. All these statistics would suggest benefit to receiving chemotherapy and radiation after surgery for this particular type of cancer.

The authors concluded, "Our results demonstrate that local/regional radiotherapy plus Fluorinated Pyrimidine-based chemotherapy administered as adjuvant (post operative) treatment significantly improves overall and relapse free survival among patients with gastric cancer. Although this therapy may be delivered safely, radiation oncologists must be familiar with the proper techniques for delivery of upper abdominal radiation in patients who have undergone gastrectomy, and the maintenance of adequate nutrition during therapy is essential. This study also indicates that lymphadenectomy is the most common type of lymph node dissection performed in the United States during resection for gastric cancer. Adjuvant treatment with Flurouracil plus Leucovorin and radiation should be considered for all patients with high risk gastric cancer."

This study is important because gastric carcinoma is a common malignancy. The improvement in cancer free survival is significant. Therapy is generally well tolerated and should be discussed with each person, their family and attending physicians. Historic studies did not have similar conclusions. Many people will likely receive chemotherapy and radiation after surgery for gastric cancers. It should be considered by all. It's up to each person - guided by family and physicians - to select what treatment one desires as part of the Informed Consent process.