

## LOOKING AT BULKY CERVIX CANCER

The importance of cervix cancer is that it can be a fatal disease that is usually preventable and often cured. It affects thousands of women in America and tens of thousands world-wide. Treatment advances that increase survival will obviously have an impact on many women and their families.

Bulky cervix cancers are certainly not unusual. Bulky describes the cancerous mass in size. Large or bulky Stage IB cervix cancer have worse local control and worse survival than other smaller Stage I cancers. Local control means the cancer is contained in the area where it originated. Similar stage means the patient has about the same extent of cancer. The staging system allows physicians and patients to compare results and treatments in a more orderly fashion.

There has always been a big dispute on whether surgery should be used for these bulky cancers in an attempt to improve local control.

A group of gynecologic oncologists who study cancer issues previously reported that removal of the uterus (hysterectomy) did not improve survival but did improve local control. In an attempt to determine the best method of treatment for women with bulky but localized, cancers researchers led by Keys et al, wrote a report published in the prestigious New England Journal of Medicine evaluating the best treatment for cervix cancer - like these.

Women with cervix cancer of Stage IB were entered into this study. The minimum diameter in the cancer had to be 4 centimeters (about one and one-half inches) to participate. Women could have no evidence of lymph node involvement or suspicion of cancer elsewhere in the body.

Some women had removal of lymph nodes but this was optional. Patients in general had good performance status or overall function. Women were excluded if thought unable to complete therapy.

Patients underwent external beam radiation, implant therapy and hysterectomy. Half the patients undergoing this treatment were to receive weekly Cisplatin chemotherapy during radiation.

Pelvic radiation was administered using 4 fields, that is, one field from the front, back, right and left side. Daily treatment doses were 180 or 200 rad delivered five days a week over about five weeks for a total dose of 4500 rad. Rad is a measurement of radiation dose.

Brachytherapy or radiation given within and about the cervix was prescribed as well. Cisplatin chemotherapy was given once a week. The dose was  $40\text{mg/m}^2$ . This prescription gives larger women a greater dose of chemotherapy. A maximum of 6 chemotherapeutic treatments were delivered. The hysterectomy was done within six weeks after radiation. The body of the uterus and cervix were removed.

The patients were entered into the study between February 1992 and April 1997. Overall 374 patients entered this study in 48 institutions. Evaluation surgically of the draining lymph nodes in the periaortic area (in the abdomen about the major blood vessel) was done on thirteen patients or 7% assigned to radiation alone in 14 patients or 8% assigned to radiation and Cisplatin. Hysterectomy was performed after radiation in 168 patients or 90%.

The authors noted that there were more patients in the radiation alone group who refused surgery compared to those in the combined modality group. Also, more people had recurrence in the radiation group than in the radiation plus chemotherapy group.

Furthermore, the authors noted there were more uteruses removed that had no detectable cancer in the group receiving combined treatment compared to those receiving radiation alone. The exact numbers were 52% versus 41%, respectively. Statistical analysis was performed and showed a statistical significance to this. One would expect better results if all the cancer was gone by pathologic analysis after chemotherapy and radiation.

The authors noted there were no treatment related deaths. Thirty five percent in the combined modality had moderate or severe adverse effects compared to 13% in the group having radiation alone. Most side effects included lowering of the blood counts or gastrointestinal effects.

Cancer recurred in 69 patients or 37% having radiation alone and in 38 patients or 21% having radiation plus chemotherapy. This meant there were fewer recurrences in those receiving chemotherapy plus radiation therapy versus radiation therapy alone.

Freedom from recurrence was greater in patients having chemotherapy and radiation therapy compared to radiation therapy alone. Forty nine patients or 26% having radiation alone died of cervix cancer. Twenty seven patients or 15% having chemotherapy and radiation therapy died. This would suggest the protective or beneficial effects of combined modality treatment - chemotherapy plus radiation.

The authors noted the three year survival rate was 74% in the group having radiation alone and 83% in the group having chemotherapy and radiation therapy together.

The authors concluded that "The five randomized studies of cervical cancer that we have discussed involved different stages of cervix cancer and combinations of treatment, but that they share a common result: all five studies found that concomitant treatment with Cisplatin and radiotherapy led to better outcomes than radiotherapy alone on combination of treatments that did not include Cisplatin. This remarkable consistency offers a compelling reason to consider Cisplatin therapy in combination with radiotherapy as a new standard of care for patients with bulky Stage IB, Stage IIB through IVA and high risks cervix cancer."

In the accompanying editorial by Gillian Thomas it is noted that "It is reasonable to suggest that Cisplatin based chemotherapy - most likely consistent weekly Cisplatin - should be given concurrently with radiotherapy. One must also keep in mind that the reported improvements in survival are associated only with concurrent chemotherapy and not with neo-adjuvant chemotherapy (chemotherapy given before or after radiotherapy). This information is of great importance to women with cervix cancer. Combined modality treatment means better outcome.