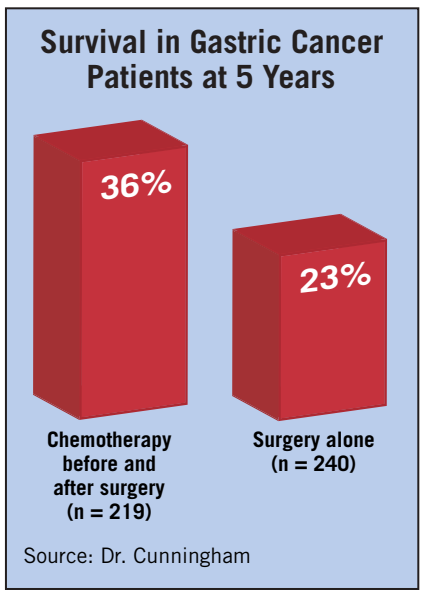
Chemotherapy Improves Gastric Cancer Survival

BY JANE SALODOF MACNEIL
Southwest Bureau

ORLANDO — Gastric cancer patients who received perioperative chemotherapy showed a 13% absolute improvement in 5-year survival in a large phase III trial sponsored by the United Kingdom's Medical Research Council.

Of the patients who received chemotherapy before and after surgery, 36% were alive 5 years after diagnosis, whereas only 23% of a control group randomized to surgery alone lived that long, investigator David Cunningham, M.D., reported at the annual meeting of the American Society of Clinical Oncology.



The chemotherapy regimen downstaged primary tumors and significantly improved progression-free survival as well, said Dr. Cunningham of the Royal Marsden Hospital in Surrey, England. He reported recurrences in 62% of the control group but in only 42% of patients who received perioperative chemotherapy.

The Medical Research Council Adjuvant Gastric Infusional Chemotherapy (MAGIC) trial enrolled 503 patients with operable cancer of the stomach and lower esophagus from July 1994 to April 2002. The trial randomized 253 patients to surgery alone and 250 to receive surgery plus three preoperative and three postoperative cycles of chemotherapy.

The chemotherapy regimen contained an intravenous bolus of 50 mg/m^2 of epirubicin and a 4-hour infusion of 60 mg/m^2 of cisplatin, both given on the first day of each 21-day cycle. In addition, patients received a continuous infusion of 200 mg/m^2 of 5-fluorouracil every day of each cycle.

Fewer patients in the chemotherapy arm proceeded to surgery: 219 patients (about 88%) vs. 240 patients (95%) in the control group. Yet more chemotherapy patients had operations that were deemed curative: 169 patients (about 79%) compared with 166 patients (about 70%) who had no chemotherapy.

Postoperative deaths (6%) and complications (46%) were the same for both groups, as was the median postoperative hospital stay (13 days).

Postsurgery pathology showed the chemotherapy patients had a smaller maximum tumor diameter (median 3 cm vs. 5 cm in the control group). The chemotherapy patients with gastric tumors were more likely to have less advanced disease: 52% were classified as T1 or T2 vs. 38% of the control group. They were also less likely to have more advanced nodal status: 16% were classified as N3 or N4 vs. 29% of the controls.

Median survival was calculated as 24 months with chemotherapy and 20 months with surgery alone. The unadjusted hazard ratio for death was 0.75 in the chemotherapy arm. Progression-free survival was also superior, with a hazard ratio of 0.66 favoring chemotherapy.

Survival results were based on an intent-to-treat analysis at a median follow-up greater than 3 years. In all, 90% of patients were followed 2 or more years or until death.

In response to an audience question, Dr. Cunningham declined to claim that the trial established perioperative chemotherapy as a new standard. Surgery alone has been standard in Europe, he said, whereas postoperative chemoradiation has been common in the United States since its benefits were reported in another standardized trial (N. Engl. J. Med. 2001; 345:725-30).

"It is difficult to compare and contrast the two different strategies, but I think what the study does do is offer us the option of two different strategies for patients with this disease—either perioperative chemotherapy or surgery and then postoperative chemoradiation," he said. "And maybe combining those strategies can improve outcomes."

Dr. Cunningham rejected a suggestion that patients in the MAGIC trial's control arm had poorer survival than did patients in other adjunctive therapy trials. He said these groups could not be compared, because the MAGIC trial enrolled "all comers," whereas adjunctive therapy trials enroll only patients who have had successful operations.

"There hasn't been much improvement in outcome [for gastric cancer patients until now], but with these multimodalities we are hoping there will be," Dr. Cunningham told this newspaper. He described the current outlook for patients with non–colorectal gastrointestinal cancers as "pretty grim," but predicted that current investigations would soon lead to "massive" improvement.

In a discussion of the MAGIC trial, Robert J. Mayer, M.D., said the results "are convincing, validating the concept of perioperative chemotherapy." What remains unclear, said Dr. Mayer, director of the center for gastrointestinal oncology at the Dana-Farber Cancer Institute in Boston, is which chemotherapy regimen is the best combination, not only for perioperative chemotherapy but also for postoperative chemoradiation. ■

Most Gastric Cancer Patients Don't Get Adequate Staging

BY JANE SALODOF MACNEIL
Southwest Bureau

ORLANDO — Two-thirds of gastric cancer patients still do not receive an adequate lymph node assessment for staging of their disease prior to surgery, Natalie G. Coburn, M.D., reported at the annual meeting of the American Society for Clinical Oncology. According to an analysis of 11,602 U.S. patients operated on from 1988 through 2001, only 27.6% had at least 15 nodes removed for examination, said Dr. Coburn of Princess Margaret Hospital and the University of Toronto.

The American Joint Commission on Cancer changed its guidelines in 1997 to make 15 nodes the standard for assessment. Though the Canadian investigators found some improvement subsequently, only 32.7% of cases from 1998 to 2001 were in compliance.

Dr. Coburn reported the median number of lymph nodes assessed was nine, with wide variation among the nine geographic regions included in the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) database.

Hawaii had the best results. A median of 15 lymph nodes were examined, and 52.5% of patients received care that met the standard for adequate assessment. That state also had the best median survival (26 months) and the best 5-year actuarial overall survival (33.4%).

In contrast, Utah had the worst record. The median number of lymph nodes examined was six, and only 17.5% of patients received an adequate assessment. Utah's median survival was the lowest (15 months), as was its 5-year actuarial overall survival (16.2%).

"Patients who had more adequate surgery and lymph node assessment had better outcomes," Dr. Coburn said at a press briefing, noting that variations in the number of lymph nodes collected correlated with disparities in survival.

Dr. Coburn reported a variety of factors affected the chance of receiving an adequate lymph node assessment. Better odds ratios (ORs) were associated with the following:

- Year of diagnosis (1998-2001, OR 1.4).
- Female gender (OR 1.3).
- Asian (OR 1.4-1.8) or African American (OR 1.4) descent.
- Tumor stage more advanced than T1 (OR 1.3-1.7).
- Increase in grade from well differentiated to undifferentiated (OR 1.4-1.8).

Patients were more likely to have an adequate assessment if they had a major surgery such as total resection (OR 1.8) or en bloc resection (OR 1.9). Patients under the age of 74 also were more likely to have an adequate assessment.

Although only a small number of patients had neoadjuvant radiation, they had lower odds of an adequate lymph node assessment (OR 0.2). Other investigators have reported similar results, according to Dr. Coburn. "They feel it's due to radiation changes in the surgical bed," she said.

Many hazard ratios (HRs) for death reflected the odds for adequate assessment. Older patients were more likely to die (HR 1.4). Japanese and other Asian Americans (HR 0.82) were less likely to die, as were women (HR 0.83). However, risk of death also increased with higher tumor stage (HR 1.4-3.4) and grade (HR 1.4), she said.

Patients with total resections had a better hazard ratio (0.88) than did those with distal resections, but the odds of dying were higher with gastrectomy (HR 1.2) and en bloc surgery (HR 1.12). Neoadjuvant radiation did not have an effect on hazard ratios, but adjuvant radiation reduced risk slightly (HR 0.9).

The investigators calculated that having an adequate number of lymph nodes removed for assessment reduced the risk of death by 14% (HR 0.86). ■

Contrast-Enhanced Intraoperative Ultrasound Helps Find Liver Tumors

BY ALICIA AULT
Contributing Writer

CHICAGO — Contrast-enhanced intraoperative ultrasound identifies more liver tumors than does the imaging technology when it is used in a conventional manner, which may increase the chances for successful surgery or prevent unnecessary surgery, Marco Montorsi, M.D., said at the annual meeting of the Society for Surgery of the Alimentary Tract.

Dr. Montorsi, of the University of Milan, said he and his colleagues hoped to increase the tumor detection rate achieved with intraoperative ultrasound (IOUS), which has 82% sensitivity in detecting liver metastases from colorectal cancer.

From September 2003 to November 2004, 57 patients at the University of Milan had a liver resection and underwent both IOUS and the contrast-enhanced procedure, which involved 2.4 mL IV of sulfur-hexafluoride microbubbles.

Of the 57 patients, 34 had hepatocellular carcinoma (HCC), and 23 had colorectal metastases. Contrast-enhanced ultrasound provided new data about 21 of the 57 patients. For seven patients with HCC, the contrast did not confirm as malignant the new nodules found by conventional imaging. In these cases its use prevented surgery, Dr. Montorsi said. In four patients, contrast-enhanced ultrasound confirmed malignancies detected by IOUS, and in two it fully confirmed as HCC the additional lesions detected by IOUS.

In patients being evaluated for colorectal metastases, the contrast found new lesions missed by IOUS in four patients and confirmed additional lesions in three patients, Dr. Montorsi said. ■