Stage III Colon Cancers

Why Adjuvant Chemotherapy Is Not Offered to Elderly Patients

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Hypothesis: Adjuvant chemotherapy is not offered to elderly patients with stage III colon cancer.

Design: A retrospective review of hospital and office records.

Setting: A suburban community hospital.

Patients: The medical records of 69 patients with stage III colon cancer were reviewed. All identified from the Tumor Registry at Jersey Shore Medical Center, Neptune, NJ, were included in this study.

Results: Thirty-five patients (51%) did not receive adjuvant chemotherapy. After adjusting for age, women were 5.8 times less likely to receive chemotherapy ($P = .002$). Patients not receiving chemotherapy were significantly older (78.7 vs 70.4 years; $P = .003$) than those who received adjuvant chemotherapy. There was no relation found between the year of diagnosis and the administration of chemotherapy. There were 4 major reasons for not receiving chemotherapy: (1) not offered ($n = 12, 34%$), (2) refused ($n = 11, 31%$), (3) too old ($n = 7, 20%$), and (4) significant concomitant disease ($n = 5, 14%$).

Conclusions: A large group of elderly patients who had been surgically treated for colon cancer and who were eligible for adjuvant chemotherapy either were not referred for treatment or refused treatment. This suggests a bias on the part of surgeons, primary care physicians, and patients against the use of chemotherapy in elderly patients.


C OLORECTAL carcinoma is the most common gastrointestinal tract malignant condition in the United States. It is estimated that more than 50% of patients who are diagnosed as having this malignant condition will eventually die from metastatic disease. In 1989, a randomized prospective trial\textsuperscript{1} was published, showing increased survival in patients with stage III cancer who received fluorouracil and levamisole hydrochloride compared with a nontreatment control group. In 1990, a larger series\textsuperscript{2} confirmed this observation. Subsequently, endorsement of this treatment regimen by a National Institutes of Health consensus study\textsuperscript{3} led to the recommendation that all patients with stage III cancer should be treated with adjuvant chemotherapy. While this disease affects young adults, it is increasingly seen in elderly patients, and the role of adjuvant chemotherapy in elderly patients has been addressed only to a limited degree. In a 1993 review from Monroe County,\textsuperscript{4} New York, the calculated early dose intensity was significantly less in patients aged 75 years and older compared with patients younger than 75 years. Since cancer is a disease of aging, the need for chemotherapy in elderly patients is an increasingly important issue. This study assesses the use of adjuvant chemotherapy in an aging population from the time when the initial recommendation for therapy with fluorouracil and levamisole was made.

RESULTS

PATIENT DEMOGRAPHICS

Seventy-six patients had been treated for stage III colon cancer during the 8-year period since the Tumor Registry had been collecting data. Six patients who died in the early perioperative period were excluded from the study. No data were available for 1 patient who had been initially treated at another hospital. Sixty-nine patients, therefore, were further examined. The patients’ ages ranged from 40 to 97 years (mean age, 74.7 ± 11.8 years). Fifty-
eight patients (84%) were aged 65 years or older. Twenty-eight of the patients were men (mean age, 74.2 ± 11.9 years), and 41 were women (mean age, 75.0 ± 11.9 years).

SEX AND TREATMENT

Thirty-four patients (20 men and 14 women) received treatment, 49% of the 69 patients examined. There was a significant difference between the likelihood of treatment based on whether the patient was a man or a woman (χ² test, \( P = .002 \)). After adjusting for age, the odds ratio was 5.8 (95% confidence interval, 1.9-18.4), i.e., there was a 5.8 times greater chance of male patients receiving treatment than female patients, if they were the same age.

AGE DISTRIBUTION AND TREATMENT

The age and sex of each treatment status, with the mean age with 1 SEM, is presented in the Figure. The median age of the treatment group (74 years) was lower than that of the nontreatment group (80 years). The mean age of the nontreatment group was significantly greater than that of the treatment group (78.7 ± 10.9 vs 70.4 ± 11.3 years; \( P = .003 \)). The mean age difference was 8.3 years (95% confidence interval, 3.0-13.6).

**PATIENTS AND METHODS**

All patients with stage III colon cancer from January 1, 1989, through December 30, 1996, enrolled in the Tumor Registry at Jersey Shore Medical Center, Neptune, NJ, were included in this study. Patients were considered to be in the “treatment group” once they were referred to an oncologist and began chemotherapy, regardless of whether the patient received the target dose. The management of these patients formed the basis of this study. Hospital records and individual records from physicians' private offices were reviewed to complete this study. The results are reported as the mean ± SD. Differences in the distribution of characteristics between groups were studied with the use of the χ² test for categorical variables and the t test for continuous variables. Multiple logistic regression analysis was used to assess the significance of variables while controlling for potentially confounding variables. The odds ratio and 95% confidence interval were estimated. All tests of statistical significance were 2-tailed. Differences were considered significant at \( P = .05 \).
RELATION OF THE YEAR OF DIAGNOSIS AND ADJUVANT CHEMOTHERAPY

The relatively small number of patients receiving chemotherapy may have been due to a failure on the part of the treating surgeons to stay current with advances in adjuvant chemotherapy. If this were true, there should be an increase in the number of patients referred for chemotherapy over time. To analyze this possibility, the year of diagnosis and the treatment management were reviewed. There was no trend toward an increase in the use of adjuvant chemotherapy during the 8 years of the study; patients were consistently referred for treatment from the time of the original study advocating adjuvant chemotherapy.1

RECURRANCE AND TREATMENT

The effect of treatment on prevention of recurrence was assessed; recurrence occurred in 14 (20%) of the 69 patients in the study. Five (14%) of the 35 patients in the nontreatment group and 9 (26%) of the 34 patients in the treatment group developed recurrent colon cancer. There was no significant difference between the groups ($\chi^2$ test, $P = .21$). The disease-free duration from surgery was compared. There was no significant difference between the 2 treatment groups (log-rank test, $P = .50$).

REASONS FOR NO THERAPY

Thirty-five (51%) of the 69 patients did not receive chemotherapy for various reasons (Figure). Seven patients (20% of the 35 not receiving treatment) were deemed too old, according to the medical record. The mean age of these patients was 87.3 ± 3.0 years. In 5 patients (14% of the 35 not receiving treatment), significant concomitant disease justified the lack of a consultant. (Three patients had significant cardiac disease, 1 had dementia, and 1 had lung cancer.) Twenty-three patients had no significant medical reason for not receiving adjuvant chemotherapy. Eleven patients (31% of the 35 not receiving treatment) (mean age, 78.6 ± 7.6 years) refused to see an oncologist or failed to follow up with their oncologist for treatment. In 2 of these 11 patients, while treatment was offered, the patients’ visit was so long after surgery that treatment was considered to be ineffective and, therefore, not given. In 12 patients (34% of the 35 not receiving treatment) (mean age, 75.3 ± 14.2 years), no evidence was found that chemotherapy was either offered or even discussed with the patient.

COMMENT

The benefit of adjuvant chemotherapy for colon cancer was first documented in 1989 in a trial of 400 patients and subsequently was confirmed in a large multicenter trial in 1990 involving more than 1200 patients. Since that time, adjuvant chemotherapy has become the standard of treatment for locally advanced (stage III) colon cancer.2 Moertl and colleagues2 showed conclusively that combination therapy reduced the recurrence rate (41%) and the mortality rate (33%) from colon cancer. The data presented herein do not demonstrate this recognized benefit of adjuvant chemotherapy; however, the sample size is too small to make any statistically reliable conclusions.

A recent survey of the management of elderly patients with colorectal carcinoma observed that only 5% of patients older than 80 years received chemotherapy compared with 20% of patients aged 80 years or younger.3 The data presented herein indicate that one third of our patients were not offered chemotherapy either by the surgeon or by a consulting oncologist. Monmouth County, New Jersey, has many retirement villages; consequently, 58 (84%) of the 69 patients in this study were older than 65 years. The concern of giving chemotherapy to this elderly population may have played a significant role in the decision making.

It has been shown that, in an aging population, patients do not tolerate their calculated dose of chemotherapy.4 It is unclear whether this subpopulation of patients obtains any benefit by not receiving their entire dose of chemotherapy. The risk of chemotherapeutic agents and the benefits to elderly patients have been the subject of limited study, especially as they relate to adjuvant therapy. It is recognized that the concerns of elderly patients are not integrated into clinical trials,3 and this lack of concern is reflected by the data presented herein. Changes in drug pharmacokinetics when treating patients with altered renal function and impaired hepatic metabolism significantly add to the risk of therapy.5 Since elderly patients are more likely to have some degeneration of liver or kidney function, the risk of treatment is increased. However, age itself without comorbid conditions does not increase the risk of adjuvant therapy, especially if the patient has successfully recovered from surgery. The most common toxic complications of adjuvant chemotherapy documented by Moertl and colleagues2 were stomatitis, diarrhea, and nausea. Myelosuppression, the most common and most lethal complication, is not commonly associated with the use of fluorouracil and leucovorin calcium or levanisole. A recent study comparing a population of patients aged 70 years or older with patients younger than 70 years showed no increase in the toxicity rates of chemotherapy in the elderly patients but similar benefits regarding disease-free survival.

The race and sex of a patient has been recently shown to influence subsequent treatment.6 The nature of the bias recognized was not identified but was thought to be a result of subconscious perceptions rather than a deliberate action. Similarly, we cannot address the nature of the bias demonstrated by our data but recognize that there was a bias on the part of the female and elderly patients who refused treatment and the physicians who failed to refer these patients to an oncologist.

While the failure to reach target dosing,4 the failure to give adjuvant therapy,8 and the concerns of increased toxicity of chemotherapy in the elderly population6 have all been identified, no study, to our knowledge, has as yet identified the reasons why this patient population does not receive therapy. The data presented herein indicate that many patients and their physicians do not support this treatment. The fact that a significant percentage of
patients were not offered or refused treatment indicates that there is a significant bias on the part of the patients or their referring physicians against chemotherapy and suggests that an educational program targeted at this group may increase the rate of therapy.

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REFERENCES


