

Stage III colon cancer at Baylor University Medical Center at Dallas and the Baylor Sammons Cancer Center: experience from 2000 to 2004

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Colon cancer remains a major cause of cancer-related morbidity and mortality. In the USA, it is estimated that 106,680 new cases will be diagnosed and that 55,170 deaths will be attributed to the disease in 2006 (1). The stage of disease at the time of diagnosis is the single most important factor for predicting survival from the disease. In early stages, colon cancer is eminently curable, with expected 5-year survival rates of 90% or better. However, if the disease is more advanced at the time of diagnosis, the outlook is not nearly as favorable. In patients with advanced or metastatic disease at presentation, the chance of 5-year survival drops below 10% (2).

Colon cancer is often asymptomatic or minimally symptomatic in the early stages of the illness, especially when the malignancy arises within the right side of the bowel. With appropriate screening, however, the disease can be discovered in the precancerous stage or in the earlier stages of cancer, when appropriate management offers an improved likelihood of cure. Unfortunately, studies have documented a low overall compliance with recommendations for colon cancer screening in the USA (3). Ongoing research continues to focus on understanding the obstacles to screening and improving compliance.

At the time of diagnosis, clinical evaluations including physical examination and radiographic studies can determine if the colon cancer has spread beyond the regional tissues and lymph nodes. Seventy-five percent of patients are diagnosed before such spread, and in those patients surgical resection remains the mainstay of curative therapy. Analysis of the surgical specimen provides critical information regarding the pathologic stage of the cancer. In colon cancer, the stage is determined by the depth of invasion of the tumor through the bowel wall (T stage), the presence of local lymph node involvement (N stage), and the presence of distant spread or metastasis (M stage). Patients who have evidence of tumor in the local lymph nodes but no signs of additional spread are categorized as stage III. Recently, three additional substages (IIIa, IIIb, and IIIc) have been applied to this group of patients, reflecting the heterogeneity in prognosis seen among these patients (4).

The role of postoperative or adjuvant chemotherapy has been clearly established in patients with surgically resected stage III colon cancer. Several large randomized trials have repeatedly demonstrated the benefits of this treatment, and in 1990 the

National Institutes of Health Consensus Conference recommended adjuvant chemotherapy for all patients with stage III colon cancer (5). One of the first trials to unequivocally demonstrate the advantages of adjuvant chemotherapy for patients with stage III colon cancer was Intergroup Trial 0035 (6), which demonstrated a significant reduction in the rates of cancer recurrence as well as a significant improvement in the survival rates of patients who were randomly assigned to receive 1 year of postoperative 5-fluorouracil (5-FU)-based chemotherapy. Since that publication, several trials have reported similar findings (7-9).

Newer chemotherapy agents have been studied in an effort to add to the convenience and efficacy of adjuvant therapy in patients with stage III colon cancer. Two such agents—capecitabine (10, 11) and oxaliplatin (12, 13)—were shown to be effective in stage IV colorectal cancer and were then tested in patients with stage III disease. Capecitabine, an orally administered prodrug that is converted to the active cytotoxic agent 5-FU, was studied as postoperative therapy in patients with stage III colon cancer in the X-ACT trial: 1987 patients were randomly assigned to receive 5-FU plus leucovorin administered intravenously for 6 months or capecitabine administered orally for 6 months. The two regimens were equivalent in their efficacy, with the toxicity profile and convenience of administration favoring the orally administered capecitabine (14).

The combination of oxaliplatin with infusional 5-FU and leucovorin, a therapeutic regimen known as FOLFOX, was studied in patients with stage III colon cancer in the large MOSAIC trial. European investigators demonstrated a better cancer-free survival rate in patients treated with FOLFOX than in those treated with 5-FU plus leucovorin alone (15). Another trial from the National Surgical Adjuvant Breast and Bowel Project involved 2407 patients with stage II or III colon cancer who were randomly assigned to postoperative treatment with standard 5-FU and leucovorin alone or the same regimen of 5-FU and leucovorin plus oxaliplatin. Again, the patients in

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Table 1. Histologic subtype of colon carcinoma at Baylor Sammons Cancer Center from 2000 to 2004

Subtype	No. of patients
Signet ring cell carcinoma	2
Mucin-producing adenocarcinoma	7
Mucinous adenocarcinoma	6
Adenocarcinoma in tubulovillous adenoma	2
Adenocarcinoma in villous adenoma	3
Neuroendocrine carcinoma, not otherwise specified	1
Carcinoid	1
Adenocarcinoma in adenomatous polyp	1
Adenocarcinoma, not otherwise specified	107

Table 2. Location of primary tumor in patients with stage III colon cancer treated at Baylor Sammons Cancer Center from 2000 to 2004

Site	No. of patients
Colon, overlapping lesion	6
Colon, sigmoid	21
Colon, descending	11
Colon, splenic flexure	6
Colon, transverse	9
Colon, hepatic flexure	9
Colon, ascending	43
Appendix	1
Cecum	24

the oxaliplatin group experienced a better 3-year cancer-free survival rate than those assigned to treatment with 5-FU and leucovorin alone (78% vs 73%) (16). The findings of this trial have confirmed the additional benefits of oxaliplatin in the treatment of patients with stage III colon cancer.

STAGE III COLON CANCER AT BAYLOR SAMMONS CANCER CENTER

Baylor University Medical Center (BUMC) and the Sammons Cancer Center represent a large tertiary referral center in Dallas, Texas. Through the tumor registry at BUMC, patients with stage III colon cancer who underwent surgical resection between January 2000 and December 2004 were identified. Of the 727 patients with colon cancer identified in the registry, 325 (45%) were found to have regional disease at the time of diagnosis, including 195 patients (27%) with stage II and 130 patients (18%) with stage III colon cancer. BUMC, then, appears to be diagnosing patients at earlier stages of disease: the 45% rate of regional disease at BUMC was higher than the 38% rate of regional disease nationally, as reported by the Surveillance, Epidemiology, and End Result (SEER) database. SEER is a national tumor registry comprising data collected in 18 regions across the USA (2).

Of the 130 patients with stage III colon cancer managed at BUMC, the median age was 68 years (range, 23–95 years), and 60 patients (46%) were male. The majority of the patients were Caucasian (95 patients, 73%), with African Americans representing 25% of the cohort (32 patients) and other racial groups representing 2% of the cohort (3 patients). The vast majority of patients (113 patients, 87% of the cohort) were found to have adenocarcinoma or adenocarcinoma with mucinous features (Table 1). Sixty-seven patients (52%) had tumors arising in the right side of the colon (Table 2). These demographic and clinical features are similar to those reported nationally.

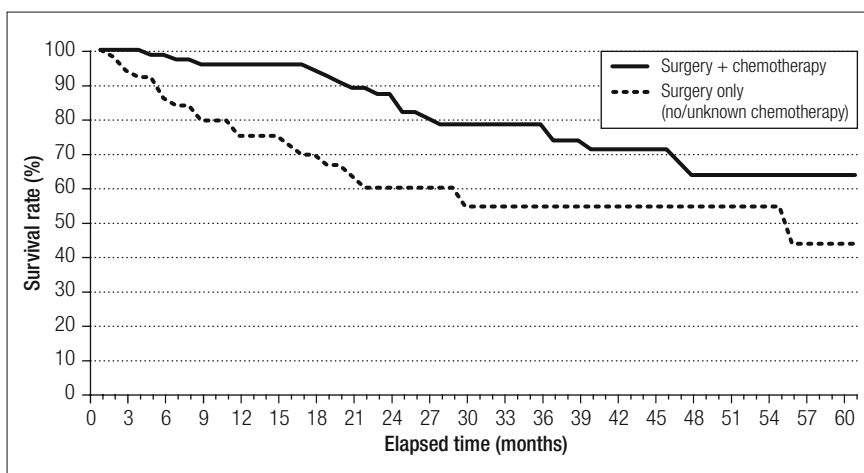


Figure. Overall survival of patients with stage III colon cancer treated at Baylor Sammons Cancer Center from 2000 to 2004 according to treatment received.

The treatment received by the cohort of patients with stage III colon cancer was evaluated. All patients had surgery. Some patients were not eligible for adjuvant chemotherapy, generally because of poor overall health. In our data, 16 patients (12%) received only surgery for their stage III colon cancer. This was a slightly older group of patients, with a median age of 70.5 years. Seventy-nine patients, or 61% of the entire cohort, received surgery followed by adjuvant chemotherapy. A small number of these patients (8 patients, 6% of the study population) also received radiotherapy as part of their treatment. For 35 of the BUMC patients (27%), the use of chemotherapy after surgery was unknown.

Nationally, 64% of patients with stage III colon cancer received adjuvant chemotherapy in 2002 (17), according to data in the National Cancer Data Base, a prospectively collected database supported jointly by the American College of Surgeons and the American Cancer Society (18). If patients with incomplete data are excluded from the analysis, then 83% (79 of 95 patients) of BUMC patients were treated with surgical resection followed by adjuvant chemotherapy, a rate higher than the national average.

In line with national data, we found a better 5-year survival rate in patients treated with surgery followed by adjuvant chemotherapy than in those treated with surgery alone (Figure). BUMC's 5-year survival rates of 64% (with chemotherapy) and 44% (without chemotherapy) were similar to those from the National Cancer Data Base, which were 66% and 50%, respectively, in 1997 (17).

BUMC and the Sammons Cancer Center continue to work towards optimizing patient access to high-level cancer care. With this, there is hope that overall patient outcomes can be improved and mirror the advances seen in large clinical trials. In the field of colon and rectal cancer, such improvement requires the collaboration of many cancer specialists, including medical oncologists, radiation oncologists, colorectal surgeons, general surgeons, and gastroenterologists. Also of importance are the nurses, nutritionists, technicians, social workers, and other experienced and caring cancer care providers who help provide a compassionate and coordinated health care delivery system. Colon cancer patients have seen recent improvements in screening and treatment options that have resulted in considerable improvements in survivorship; with ongoing research and enhanced delivery systems, these outcomes can be improved even more.

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