Result

characteristics of the patients and tumors Between August 1994 and August 2001, 872 pa-tients underwent randomization (Fig. 1). Two pa-tients declined to undergo any surgery and 7 were ineligible, leaving 863 patients for the final analy-sis. Among these patients, 53 had nonmalignant disease and 26 had stage IV disease identified at surgery (16 in the open-colectomy group and 10 in the group that underwent laparoscopically assisted colectomy). The two study groups were well bal-anced (Table 1). Only 14 patients (2 percent) revoked consent or were lost to follow-up (only 3 patients were lost to follow-up before four years).surgery

A total of 428 patients underwent open colectomy, and 435 were treated initially with laparoscopically assisted colectomy. The procedure was converted to open colectomy for 90 patients assigned to laparo-scopically assisted surgery (21 percent) (Table 2). Conversion rates did not differ significantly be-tween surgeons with a high volume of procedures and those with a low volume or between surgeons who participated early or late in the trial (data not shown).Operating times were significantly longer in the laparoscopic-surgery group than the open-colec-tomy group (150 minutes vs. 95 minutes, P<0.001). Patients in the open-colectomy group were more likely than those in the laparoscopic-surgery group to undergo concurrent resection of other organs(63 vs. 34 patients, P=0.001); malignant histologic findings were identified in these resected organs in 14 patients in the open-colectomy group, as com-pared with 6 in the laparoscopic-surgery group. Ab-dominal-wall adhesions (P=0.002) and bowel ad-hesions (P=0.001) were reported more frequently among patients in the laparoscopic-surgery group.The extent of resection was similar in both groups; bowel margins were less than 5 cm in 6 per-cent of the patients in the open-colectomy group and 5 percent of those in the laparoscopic-surgery group (P=0.52). In each group, the median number of lymph nodes examined was 12.recovery and complications

Perioperative recovery was faster in the laparoscop-ic-surgery group than in the open-colectomy group, as reflected by a shorter hospital stay (P<0.001) and briefer use of parenteral narcotics (P<0.001) andoral analgesics (P=0.02) (Table 2). There were no significant differences between the groups in the rates of intraoperative complications (2 percent in the open-colectomy group and 4 percent in the lap-aroscopic-surgery group, P=0.10), 30-day postoper-ative mortality (P=0.40), rates and severity of post-operative complications at discharge (P=0.98) and at 60 days (P=0.73), and rates of readmission (10 percent and 12 percent, respectively; P=0.27), or the rates of reoperation (less than 2 percent in each group, P=1.0). The percentage of patients receiving chemotherapy did not differ significantly between groups and paralleled the rate of stage III disease.survival and

recurrence

After a median follow-up of 4.4 years, 160 patients had had a recurrence of tumor (84 in the open-colectomy group and 76 in the laparoscopic-surgery group) and 186 had died (95 and 91, respectively). Seventy-seven patients died before the tumor re-curred (34 in the open-colectomy group and 43 in the laparoscopic-surgery group, P=0.25). The one-sided P value for the time to recurrence in favor ofthe open procedure was 0.83, satisfying the criteria to declare the laparoscopic procedure not signifi-cantly inferior to the open procedure. As shown in Figure 2A, the cumulative incidence of recurrence among patients treated with the laparoscopic pro-cedure did not differ significantly from that for pa-tients who underwent open colectomy (two-sided P=0.32; hazard ratio for recurrence, 0.86; 95 per-cent confidence interval, 0.63 to 1.17). The estimat-ed difference in the three-year recurrence-free ratewas 2.4 percentage points in favor of the laparo-scopic-surgery group (95 percent confidence inter-val, ¡2.9 to 7.8).The overall survival rate was also very similar in the two groups (P=0.51; hazard ratio for death in the laparoscopic-surgery group, 0.91; 95 percent con-fidence interval, 0.68 to 1.21) (Fig. 3), as was the disease-free survival rate (117 events in the open-colectomy group and 118 events in the laparoscopic-surgery group; P=0.70 by the log-rank test; hazard ratio for recurrent disease in the laparoscopic-surgery group, 0.95; 95 percent confidence interval, 0.74 to 1.23). These findings held true for patients with any stage of cancer: there were no significant differences between treatment groups in the time to recurrence (Fig. 2), disease-free survival, or overall survival for any stage (Fig. 3). Conclusions drawn from the two sensitivity analyses (one conducted strictly according to the intention to treat and the other excluding patients with stage IV disease) were virtually identical (data not shown). The absence of a difference in the time to recurrence, disease-free survival, and overall survival persisted in multivari-ate analyses adjusted for the stratification factors. Tumor recurred in surgical wounds in three pa-tients: two in the laparoscopic-surgery group (0.5 percent) and one in the open-colectomy group (0.2 percent, P=0.50).

Methods

patients

The details of the design and methods for this non-inferiority trial have been reported previously.8-10 In-clusion criteria were a clinical diagnosis of adeno-carcinoma of the colon (histologic confirmation was required at surgery), an age of at least 18 years, and the absence of prohibitive abdominal adhe-sions. Exclusion criteria included advanced local or metastatic disease, rectal or transverse colon cancer, acute bowel obstruction or perforation from cancer, and severe medical illness. Inflammatory bowel dis-ease, familial polyposis, pregnancy, or concurrent or previous malignant tumor also precluded enroll-

ment. The study was approved by the institutional review board of each participating center, and all patients provided written informed consent.

Table1

Table 1. Baseline Characteristics of the Patients and Tumors.*Characteristic*

Open

Colectomy

(N=428)

Laparoscopically

Assisted Colectomy

(N=435)

Age — yr

Median

Range

69

29–94

70

28–96

Female sex — no. (%) 220 (51) 212 (49)

American Society of Anesthesiologists

class — no. (%)

1 or 2

3

367 (86)

61 (14)

373 (86)

62 (14)

Location of primary tumor — no. (%)

Right side of colon

Left side of colon

Sigmoid colon

232 (54)

32 (7)

164 (38)

237 (54)

32 (7)

166 (38)

*TNM stage — no. (%)**

0I

II

III

IV

Unknown

33 (8)

112 (26)

146 (34)

121 (28)

16 (4)

0

20 (5)

153 (35)

136 (31)

112 (26)

10 (2)

4 (1)

Depth of invasion — no. (%)

Submucosal, not muscle wall

Muscle wall, not serosal or perirectal

Serosal

Beyond serosa or perirectal fat, involvement

of contiguous structure

Not applicable (benign pathological

findings)

Unknown

59 (14)

76 (18)

237 (55)

23 (5)

33 (8)

0

67 (15)

105 (24)

226 (52)

12 (3)

20 (5)

5 (1)

Grade of differentiation — no. (%)

1 (Well)

2 (Moderately)

3 (Poorly)

4 (Undifferentiated)

Not applicable (benign pathological

findings)

Unknown

44 (10)

271 (63)

72 (17)

6 (1)

33 (8)

2 (<1)

36 (8)

315 (72)

51 (12)

5 (1)

20 (5)

8 (2)

No. of previous operations — no. (%)

01

>1

Unknown

233 (54)

120 (28)

37 (9)

38 (9)

246 (57)

113 (26)

41 (9)

35 (8)

3. Patient Eligibility

Required characteristics

3.11 Must have the clinical diagnosis of adenocarcinoma involving a single colon segment of the right (defined as from ileocecal valve up to and including the hepatic flexure), left (defined as from splenic flexure to junction of sigmoid and descending colon), or sigmoid colon (defined as between the descending colon and rectum [at least 15 cm from dentate]) based on the following considerations:*

– physical examination, and

– diagnostic workup (proctosigmoidoscopy and barium enema or colonoscopy).

**Final pathology must confirm this diagnosis for the patient to remain in the study.*

For multiple carcinomas, the most advanced stage lesion will be indexed.

*3.12 Consenting adult age ⩾**18 years.*

3.13 Must be able to participate in follow–up evaluations.

3.14 Must not have prohibitive scars/adhesions from previous abdominal surgery (surgeon's discretion).

3.2 Contraindications

3.21 Any of the following disease considerations:

– advanced local disease rendering laparoscopic resection not possible (based on preoperative evaluations).

– stage IV disease (based on preoperative studies).

– rectal cancer (below peritoneal reflection, lower edge of tumor <15 cm from dentate as measured by surgeon using rigid proctoscope).

– acutely obstructed or perforated colon cancer requiring urgent surgery.

– transverse colon cancer (between distal hepatic flexure and proximal splenic flexure).

– ASA classification IV: severe, incapacitating disease.

– ASA classificationV: imminent danger of death.

3.22 Associated gastrointestinal diseases that require additional extensive operative evaluation or intervention (i.e., Crohn's, chronic ulcerative

colitis, familial polyposis).

3.23 Pregnant women.

3.24 Any concurrent or previous malignant tumor (within the previous 5 years)

except superficial squamous or basal cell carcinoma of the skin or in situ

cancer of the cervix.

5. Stratification Factors

5.1 Site of primary tumor: right, left, or sigmoid colon.

5.2 Primary surgeon: designated institutional surgeon.

5.3 ASA classification (11–12): I & II versus III.

– ASA I: Healthy patient.

– ASA II: One systemic, well–controlled disease.

– ASA III: Multiple system