Egyptian Journal of Surgery Vol. (21), No. (2), April, 2002

EVALUATION OF PRIMARY RESTORATIVE COLECTOMY IN MALIGNANT LEFT-SIDED COLONIC OBSTRUCTION WITH INTRA-OPERATIVE COLONIC DECOMPRESSION FOLLOWED BY POST-OPERATIVE ADJUVANT CHEMOTHERAPY

By
A. Motamed, M.D.; Azza S Abdel Naby, M.D.*
Departments of General Surgery and Clinical Oncology and Nuclear Medicine*, Faculty of Medicine,
Mansoura University- Egypt.

There has been a trend towards one stage resection and anastomosis in obstructed left colonic cancer even in the elderly with on-table colonic lavage. The aim of this work was to evaluate the outcome in twenty two patients with obstructed left colonic cancer at or distal to splenic flexure managed by primary restorative colectomy using intra-operative colonic decompression. It was done on 22 patients at Emergency Hospital, Mansoura University from Augest 1994 to December 1996. Intra-operative colonic decompression was done on a thirty-six Fr multiperforated Nelaton tube before division of mesentery followed by radical left hemicolectomy. Anastemotic leakage occurred in one patient who died (mortality rate 4.5%). Mean time of colonic decompression was 21±3.4 minutes. Wound infection occurred in (13.6%), chest infection in (4.5%) and paralytic ileus in (4.5%). Post-operative adjuvant chemotherapy consisting of 6 courses of 5-fluorouracil (5-FU) and leucovorin (LV) was given. Primary resection and anastomosis of left colonic cancer can be achieved by colonic decompression before division of the mesentery avoiding spillage of colonic contents, improving blood supply and the tone of the colon ensuring safe and rapid anastomosis with low morbidity and mortality. The 5-year DFS and OS rates for the, whole of our group, were 42.9% and 52.4% respectively. They were related to the Dukes stage, as for Dukes' B the DFS and OS rates at 5-years were 66.7% and 83.3% respectively, while for Dukes' C patients, they were 45.5% and 54.6% respectively. For Dukes' D patients, the 2-year OS was 20% with non of the patients was alive at 5-years.

Keywords: primary restorative colectomy. Obstructed left colonic cancer. Intra-operative colonic decompression. Post-operative adjuvant chemotherapy.

INTRODUCTION

Cancer colon is an important cause of cancer-related mortality[1]. Although left sided malignant colonic obstruction is often managed by the traditional method of staged defunctioning colostomy and resection, there has been a trend towards one stage primary resection and anastomosis even in the elderly [2].

Staged resection procedures are not only poorly tolerated by many patients but also had to prolonged hospital stay and increased mortality rates. The mortality rate of colostomy closure ranges from 5-57% and a large proportion of patients may never proceed to reversal mainly because of medical problems [3 & 4].

Primary resection was facilitated either by on-table antegrade colonic irrigation [5 & 6] or intra-operative colonic decompression alone [7 & 8] as mechanical bowel preparation has shown to be unnecessary for elective colo-rectal surgery [9].

Anastomotic leakage following colorectal surgery ranges from 3.4% as high as 8%, and at least one third of

the mortality following colo-rectal surgery is attributed to leaks at anastomosis [10, 11].

Although most patients present with surgically resectable disease, an unacceptably high number of individuals develop recurrence despite appropriate local therapy. A small number of patients with recurrent disease may be cured by salvage resection of pulmonary or hepatic metastases, but the majority of patients who develop metastases will ultimately die of their disease[1]. The most important prognostic factor in determining the risk of recurrence of a colon cancer is the histopathologic stage of the tumor at the moment of resection [12]. The majority of patients with stage I disease are cured with surgery alone with a 5-year survival rate of at least 90%. Patients whose tumors invade through the muscularis propria or into pericolic structures have stage II disease which is associated with approximately 75% 5 year survival rate. Patients with stage III disease, in which there is involvement of lymph nodes, have an inferior survival in the range of 50% at 5-years[13]. Factors association increased risk in stage II disease, include complete colonic obstruction, perforation, regional implants or invasion of the tumor into adjacent organs. Within stage III disease, the number of involved lymph nodes is an important prognostic variable [14].

The goal of adjuvant systemic treatment is to improve cure rates through eradication of micro-metastatic disease in appropriate selected patients. Since many patients receiving adjuvant therapy may already be cured, minimizing toxicities of therapy is essential [1].

It has been shown that an adjuvant treatment with 5-FU and leucovorin (6-12 months) improves significantly the survival. The benefit is in the same range as that for treatment of 5-FU and levamisole [15]. Three large randomized multicenter American Trials (NSABP, NCCTG and Intergroup) have treated several thousands of patients after surgical resection of colon tumor with 5-FU and levamisole or 5-FU and leucovorin or combination of 5-FU and levamisole and leucovorin during 6-12 months. The first results of these trials do not show a significant difference in the different groups. It also seems that the treatment of 6 months is as efficient as a treatment of 12 months [16-19]. Based on these findings it can be proposed that the standard treatment of 5-FU and levamisole can be replaced by a treatment of 5-FU and leucovorin for 6 months [12].

This work was designed to evaluate the outcome in twenty-two patients with malignant obstructed left colon treated by resection, intra-operative colonic decompression and primary anastomosis, followed by 6 courses of adjuvant combination chemotherapy consisting of 5-FU and leucovorin.

PATIENTS AND METHODS

From August 1994 to December 1996, 22 consecutive selected patients (11 males and 11 females) were referred to the Emergency Hospital, Mansoura University with an acute intestinal obstruction. They were operated upon by the auther, where standard radical left hemicolectomy was done using the procedure described below. No patients were excluded and Hartmann's procedure was not done. All patients were given perioperative antibiotics: ceftriaxone 2 gram with metranidazole 500 mg I.V. every 8 hours. A thoracic epidural cather was placed at the level of thoracic 8-10 via a thoracic paramedian approach, 1% lidocaine, 0.25% bupivacaine plus 2 gm morphine, 2 ml for each pair of the segments. At laparatomy, the obstructing lesion and adjacent colon were mobilized for resection. A ten cm segment of the distended colon immediately proximal to the obstructing lesion was emptied of its contents by manually milking it proximally and placing a Kocher's clamp across the colon. A purse-string suture was placed in this 10-cm collapsed segment of the bowel between the kocher and obstructing lesion and a 36 Fr multiperforated Nelaton tube was inserted via a colotomy secured by the burse string suture. Gentle suction was applied to the Nelaton tube as the crushing clamp was removed and the Nelaton tube slid proximally into the obstructed distended colon. The colon decompressed rapidly and easily since it was distended mostly with gas and liquid feacal matter. The tube was flushed with saline when solid fecal matter was encountered. Colonic decompression took (12-25 minutes) and the Nelaton tube was withdrawn and the burse-string sutured was tied. Division of the mesentery, colon resection and primary anastomosis were performed using an inverted suture technique, two layers, interrupted, 3/0 vicryl without tension. The abdomen was closed with a thirty-two Fr Nelaton tube as a drain and was removed on the fifth post-operative day.

Early enteral nutrition on the fourth post-operative day and a continuous thoracic epidural analgesia 1/10 of the anaesthetic dose/4 hours was given for 48 hours post-operatively.

Wounds were inspected at 5 and 12 days, 4 weeks post-operatively wound infection was defined as serous or purulent discharge occurring at any time during observation. Anastomotic dehiscence was diagnosed on clinical grounds alone. Duke's staging and morbidity and mortality (within 30 days of operation) were evaluated.

All obstructed lesions were proven histologically to be adenocarcinoma. The patients were then referred to the Department of Clinical Oncology and Nuclear Medicine for

post-operative adjuvant treatment. Pretreatment evaluation included a complete history and physical examination. Patients were required to have acceptable blood and platelet count (neutrophil count ≥2000/UL platelet count ≥100.000/UL), adequate hepatic (bilirubin level ≤2 mg/dl) and renal function (serum creatinine ≤2 mg/dl). Chest x-ray, and computed tomographic (CT) scan of the abdomen. CEA and CA_{19-9} levels were assessed as a baseline before treatment. Evaluation while on protocol included weekly toxicity notation and complete blood cell count, physical examination with weight and performance status and serum chemistries before the administration of each cycle. Scan and tumour markers were repeated every 16 weeks. Colonoscopy was done every 20 weeks.

Treatment regimen:

A cycle of therapy was defined as 4 weeks, to include 5 daily treatment. All patients were to be treated as outpatients. Treatment cycles were repeated for 6 cycles. Therapy consisted of 5-fluorouracil (5-FU) 425 mg/m^2 I.V bolus daily for 5 days immediately after leucovorin, and leucovorine (LV) 20 mg/m^2 I.V. bolus daily for 5 days.

After completion of the assigned chemotherapy during the second year patients were required to undergo the aforementioned evaluations every 3 months. CEA and CA_{19-9} every 6 months, and chest radiography and barium enema or colonoscopy yearly. During the years 3-5, physical examination, and blood and serum assays were required every 6 months, and chest radiography and barium enema or colonoscopy were required yearly.

Statistical analysis:

Correlation was used to test for linear relationship between age, decompression time, operative time and hospital stay. For pathological staging: repeated measures, analysis of variants (ANOVA) was used. For F value <0.05 post HOC comparison was carried out using Newman-Keuls test. Post-operative complications were expressed in percentages. Data were expressed as mean ±S.D. P<0.05 was considered significant. Overall survival (OS) was calculated from the first day of treatment until death or the date of last follow up. Disease free survival (DFS) was calculated from the first day of treatment until disease progression. Probability of survival and disease free survival as a function of time were calculated according to the Kaplan Meier method.

RESULTS

Twenty-two consecutive selected patients were studied prospectively. Their age ranged from 20-74 years (mean 48±16.9y). These were 11 males and 11 females (Table 1). The sigmoid colon was the commonest site (54.5%) followed by the descending colon (27.3%) and splenic flexure (18.2%) (Table 2).

Dukes staging was B in 6 patients (27.3%), C in 12 patients (54.5%) and D in 4 patients (18.2%).

The mean time of colonic decompression was 21±3.4 minutes. The mean operative time was 119±32 (80-200) minutes. Post-operative hospital stay ranged from 6-18 day (mean 8±2.6 days) (Fig. 1). It was longer in Dukes' C patients (Table 3). The only anastomotic leak occurred in a 74-years old male with a sigmoid adenocarcinoma (Dukes'C). He was explored where a pelvic abscess was detected, drained and a proximal loop colostomy was done, but the patient died on the 18th postoperative day due to myocardial infraction. Operative time and hospital stay were longer in the old age . P value =0.01, 0.003 respectively (Table 4) (Fig. 2). Wound infection occurred in 3 patients, managed conservatively. Chest infection occurred in 1 patient while small bowel infarction occurred in a 63-years-old male patient on the 6th postoperative day, managed by resection anastomosis. The total incidence of complications were 36% (Table 5) (Fig. 3).

Only twenty-one patients received post-operative adjuvant chemotherapy and were evaluable for response and toxicity. There were 6 patients with Dukes' B, 11, patients with Dukes' C and 4 patients were with Dukes'D. Out of the 4 patients with Dukes'D, 2 patients have liver metastasis, one patient had liver and lung metastasis and one patient had bone metastasis for which he received palliative radiotherapy -3000cGy /3 wks- to the bony pelvis in addition to the adjuvant chemotherapy with subjective response.

The 5-year overall survival (OS) for the whole group was 52.4%, with a 5-year disease free survival (DFS) of 42.9%.

The DFS for patients with Dukes'B disease at 5 year was 66.7%, while the OS was 83.3%. For Dukes' C disease patients the DFS and OS at 5-years were 45.5% and 54.6% respectively (Fig. 4 & 5).

For Dukes'D, the 2-year survival was 20% and non of the patients was alive at 5 years.

Regarding toxicity after treatment, diarrhea was the most common side effect, encountered in 16/21 patients (76.2%); grade 3 and grade 4 occurred in only 5 (23.8%) and 1 (4.8%) patients respectively. Stomatitis and myelosuppression were found in 4 patients each. Vomiting occurred in only 2 patients. Lastly alopecia occurred in 3 patients. No patient developed hand-foot syndrome and no deaths occurred while on treatment.

Table (1): *Demographic Data*

Age	48±16.9 (20-74)
Sex: female %	11 (50%)

Table (2): *Location of the obstructing tumour n=22*

Location	Number	%
Sigmoid colon	12	54.5
Descending colon	6	27.3
Splenic flexure	4	18.2

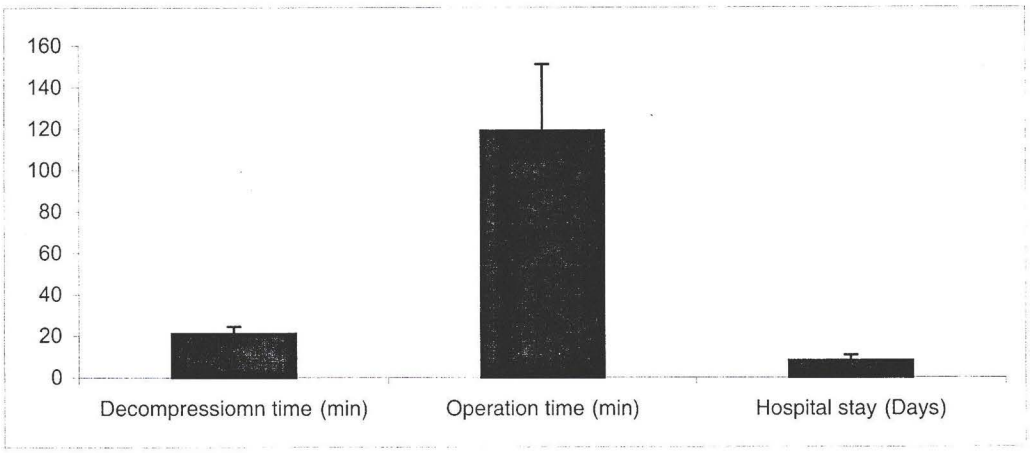

Fig. (1): Mean time of decompression (in min), operation time (in min) and hospital stay (in days).

Table (3): *Correlation of age, decompression time, operative time, and Hospital stag with the Dukes staging*

	Duke's B	Duke's C	Duke's D
Age	52± 9	48± 24	30± 16
Decompression time (min).	21± 3.5	22± 2.5	19± 4
Operative time (min)	100± 14	153± 33*	127± 28
Hospital stag (Days)	7.5± 1	9.7± 4.5	7.2± 0.8

P<0.05 significant when compared with Duke's B.

Table (4): *relationship between age, decompression time (min), operative time (min) and hospital stay (days)*

	r^2 (correction coefficient)	P value
Age and decompression time	0.09	0.16
Age and operative time	0.06	0.71
Age and hospital stay	0.27	0.01*
Decompression time and operative time	0.006	0.91
Decompression time and hospital stay	0.003	0.8
Operative time and hospital stay	0.34	0.003*

* P<0.05 positive correlation.

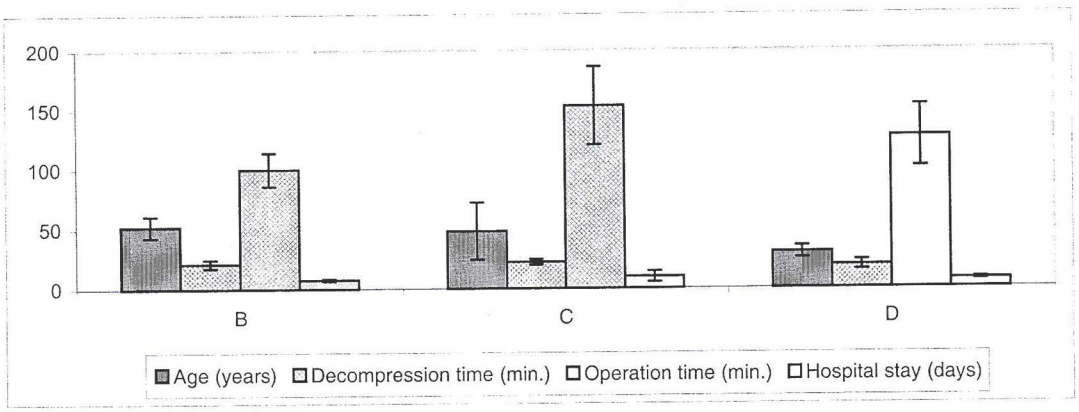

Fig. (2): Age versus decompression time, operation time and hospital stay.

Table (5): *Mortality and morbidity for obstructing left colon due to cancer n= 22*

	Number	*%*
Death	1	4.5
Anastomatic leak	1	4.5
Wound infection	3	13.6
Chest infection	1	4.5
Prolonged paralytic ileus	1	4.5
Small bowel infarction	1	4.5
Total	8	36

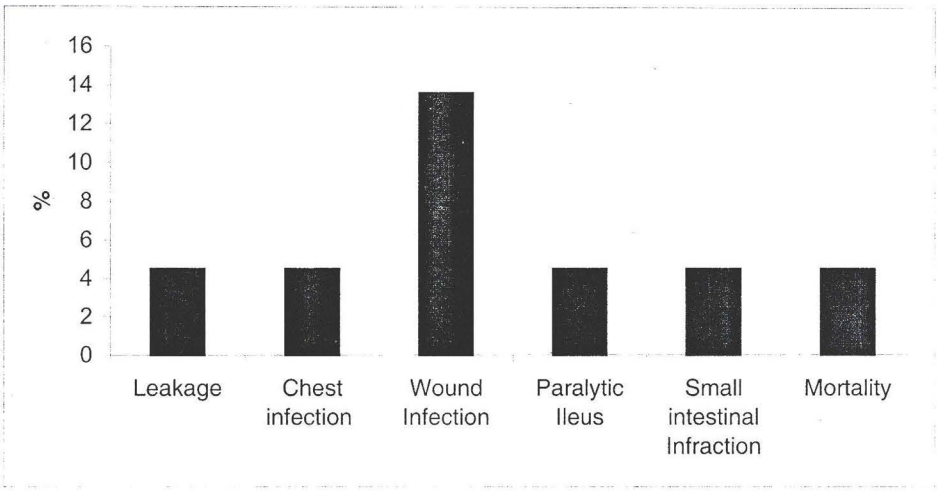

Fig. (3): Postoperative complications.

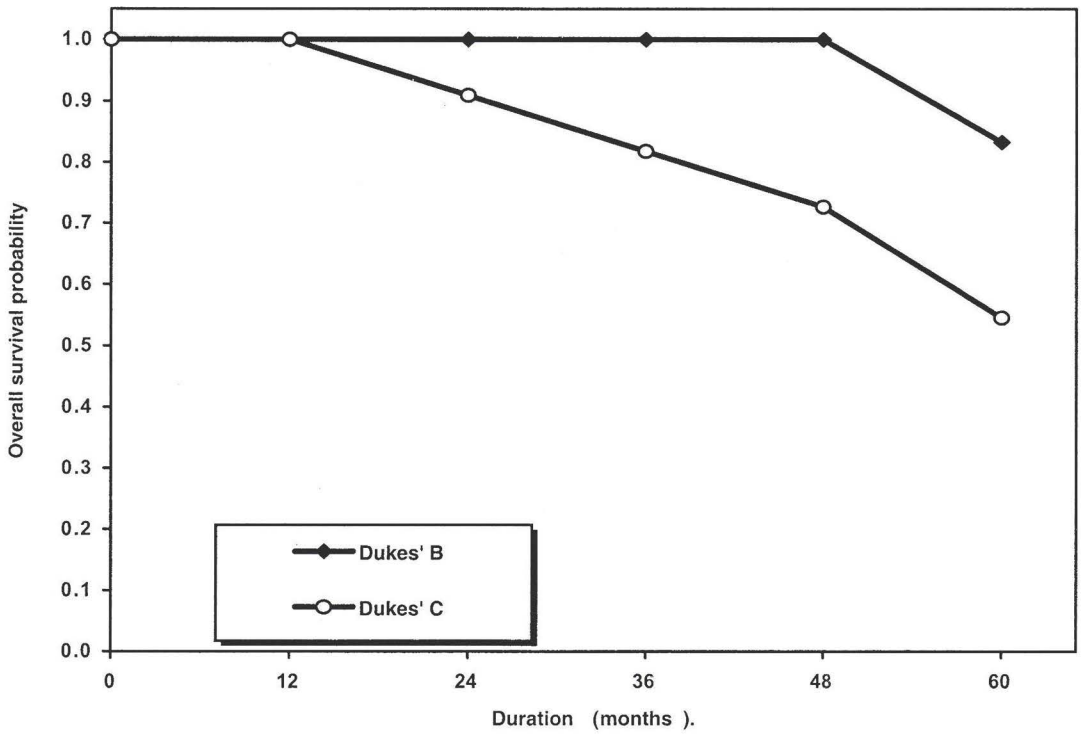

Fig. (4): Overall survival probability in patients with Dukes ' B and C lesions

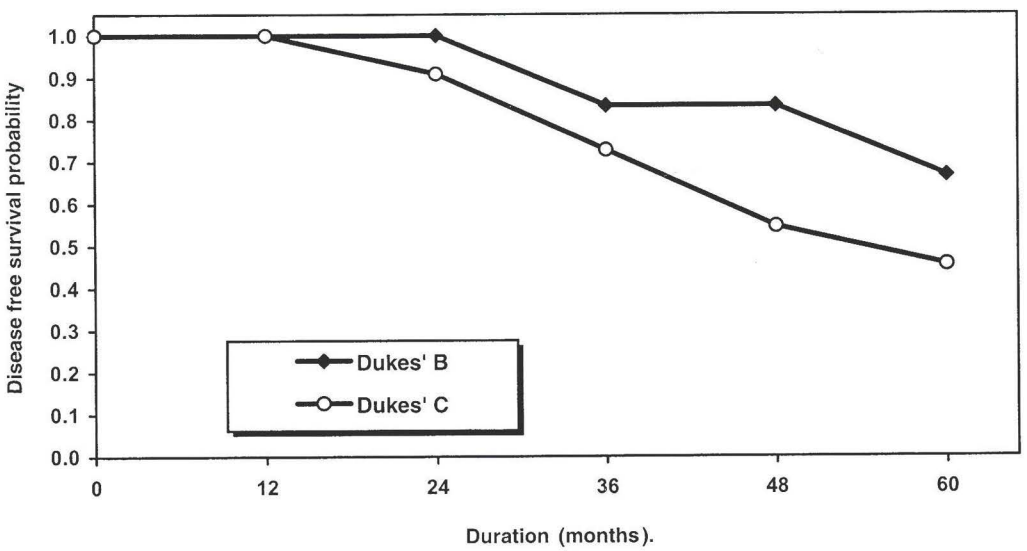

Fig. (5): Disease free survival probability in patients with Dukes' B and C lesions

DISCUSSION

Surgical resection is the initial treatment of choice for most patients with colorectal cancer. The objective is to remove the tumor and adjacent lymph nodes [20]. Primary anastomosis after on-table colonic lavage for left sided malignant colonic obstruction has the following advantages: single stage does not result in colostomy, may have lower associated morbidity and mortality rates, and shorter hospitalization than multistage procedure[2]. But per-operative colonic lavage takes more time (44 min) [21] than decompression, 12 min [8], and 21±3.4 min in our study. It also uses several liters of solution for irrigation, may be associated with more risk of spillage, fluid and electrolyte imbalance and intra-operative hypothermia [7]. Recent evidences show no clear association between failure to clean the colon thoroughly and anastomotic dehiscence [6-9].

Clinical anastomotic leak rate in emergency surgery of the left colon treated by on table lavage was 6% [8]. In our study by colonic decompression it was 4.5%. Complications rate of 10-20% was reported [22]. In our study, it was 36%.

The 30 day mortality rate was 5%[8], 8.6% [23], 10%[24], 11% [25]. In our study, it was 4% by colonic decompression.

Contraindications for resection and primary anastomosis in malignant left colonic obstruction include poor general condition, chronic corticosteroid therapy[26], fecal or advanced purulent peritonitis[6], proximal colonic damage and irresectable lesion[3] and the alternative is Hartmann's operation or colostomy [25].

Decompression of the colon is recommended as this improves the blood supply and the tone of the decompressed gut wall especially when the decompression is done before the mesentery is divided and the gut resected [5 & 8].

On the other hand, the 36 Fr Nelaton tube is multiperforated, and has a wide bore, so while freely draining the bowel gas, it is less likely to become blocked by thick liquid contents of obstructed colon [8]. This was our experience This technique was proved to be safe even in the old age. However it was associated with longer both hospital stay and operative time. This conferms what was reported by Poon et al. [2]. Even when anastomotic leakage occurred, salvage was proposed with good outcome [27], encouraging resection and primary anastomosis in obstructed left colon due to cancer [28].

Over the past two decades, the role for adjuvant therapy in colon cancer has evolved significantly and advances continue in determining the optimal regimen for use in this sitting. Combining 5-FU with other cytotoxic therapies may have necessitated decreased 5-FU doses due to excessive toxicity with combination chemotherapy. In retrospect, loss of dose intensity of the potentially more active 5-FU may explain the lack of efficacy seen in some combination chemotherapy trials [29].

In general, adjuvant chemotherapy, should be considered for patients with stage III (Dukes' C) or high risk stag II (Dukes'B) disease[1]. Patients presenting with bowel obstruction are at particularly high risk of relapse [30]. Fluorouracil-based regimens continue to be the standard in the adjuvant setting. A series of clinical trials has demonstrated that approximately 6 months of a leucovorin-containing regimen is as effective as a more prolonged therapy. The addition of levamisole to 5-FU and leucovoin (LV) has been shown to be unnecessary. While 12 months of 5-FU plus levamisole or 6 months of 5FU plus leucovorin are equally effective, the latter regimen appears preferable due to the shorter duration of therapy. Both the weekly 5-FU schedule with high dose leucovorin (LV) and the monthly 5-day schedule of 5-FU and LV are acceptable and the choice should be based on doctor or patient preference [1]. Furthermore data from randomized prospective trial suggest that 5-FU and LV is active in the adjuvant setting regardless of the schedule and duration used [31].

The 5 year DFS and OS rates for the whole of our group were 42.9% and 52.4% respectively. These results are lower than those obtained by Wolmark et al. [31] where, DFS of 65% and OS of 74% were obtained. This difference may be due to the relative small number of patients in our study and it may reflect a larger proportion of stage II (Dukes'B) patients enrolled in their study.

5-year DFS for patients with Dukes' B disease in the present study was 66.7% and OS was 83.3%. For Dukes'C patients, the 5-yearDFS and OS rates were 45.5% and 54.6% respectively. These results are lower than those obtained by Wolmark et al., [31], who found DFS and OS for patients with Dukes'B at 5 years:75% and 84% respectively, while for Dukes'C patients, DFS and OS rates 57% and 67% respectively. Nearly the same results were obtained by the NSABP trials where the DFS and OS for patients with Dukes'B disease at 5 years were 73.5% and 87% respectively while for their patients with Dukes'C, they were 55.8% and 65.1% respectively. The difference between their results and ours may be attributed to the relative small number of patients in our study and their advanced stage as all of them presented with obstruction.

For patients with metastatic colorectal cancer, trials of 5FU and leucovorin have demonstrated improved response rates and in some cases, improved quality of life and better survival [32]. In our study, hepatic metastasis was the commonest metastatic site encountered in 3 out of 4 patients. None of our patients was alive at 5-years. The 2-year OS in Dukes'D patients was 20%. These results agree with those found in other series [33]. Kemeny and Ron [34] reported that hepatic metastases are a major cause of morbidity and mortality for patients with colorectal cancer. Hepatic metastases when untreated are uniformly fatal with survival usually measured in months. Current systemic chemotherapy resulted in one year survival in metastatic colorectal cancer in 54% to 65% of patients receiving I.V. chemotherapy. The reported 2-year survival was 19-27%.

Combination of 5-FU and LV as adjuvant treatment of colon cancer is generally well tolerated. In our study, the side effects were mild, and they were comparable with those reported in other studies [1 & 31].

In conclusion, resection and primary anastomosis of the malignant obstructed left colon can be achieved by decompression of the colon before the mesentery is divided avoiding spillage of colonic contents, improving the blood supply, and the tone of the colon, ensuring a safe rapid anastomosis with low morbidity and mortality. Neither time consuming intra-operative colon irrigation, nor routine subtotal colectomy was found to be necessary.

Early enteral nutrition, continuous thoracic epidural analgesia for 48 hours post-operatively reduced post-operative infections complications and paralytic ileus.

With thoughtful selection of a treatment regimen and appropriate monitoring of toxicities, post-operative chemotherapy is a safe and effective means to increase the cure rate of surgically resected colon cancer. Although, the DFS and OS rates were lower in our patients with obstructed left colonic cancer and it was related to the Dukes stage, continued evaluation of evaluable therapies is necessary in order to continue to make meaningful advances in the treatment of colon cancer. New combination of 5-FU, CPT-II and oxaliplatin may improve the efficacy of adjuvant chemotherapy in the near future.

REFERENCES

1. Moore HCF; and Haller DG: Adjuvant therapy of colon cancer. Semin Oncol, 1999; 26 (5) October 545-555.

2. Poon RTP, Law WL, Chu KW et al.: Emergency resection and primary anastemosis for left sided obstructing colo-rectal carcinoma in the elderly. Br. J. Surg. 1998; 85:1539-1542.

3. Bakker FC, Hoitsma HFW, and Denotter G: The Hartmann's procedure. Br. J Surg 1982; 69:580-582.

4. Foster ME, Leaper DJ; and Williamson RC: Changing patterns in colostomy closure. The Bristol experience (1975-1982). Br. J Surg, 1985; 72:142-145.

5. Radcliffe AG and Audly HA: Intra-operative antegrade irrigation of the large intestine. Surg. Gynecol Obstet 1983; 156:721-723.

6. Biondo S, Jaurrieta E, Jorba R et al.: Intraoperative colonic lavage and primary anastomosis in peritonitis and obstruction. Br. J Surg. 1997; 84:222-225.

7. Nyom DCNK, Seow Choen F, leong AFPK et al.: Colonic decompression without on-table irrigation for obstructing left sided colorectal tumors. Br J Surg 1996; 83:786-787.

8. Naraynsingh N, Rompaul R, Maharaj D et al.: Prospective study of primary anastomosis without colonic lavage for patients with an obstructed left colon. Br. J. Surg. 1999; 86:1341-1343.

9. Santos JCM Jr, Batista J, Sirimarco MT et al.: Prospective randomized trial of mechanical bowel preparation in patients undergoing elective colorectal surgery. Br. J. Surg 1994; 81:1673-1676.

10. Mann B, Kleinschmidt S, and Stremmel W: prospective study of hand-sutured anastomosis after colorectal resection. Br. J. Surg. 1996; 83:29-31.

11. Alves A, Panis Y, Trancart D et al.: Factors associated with clinically significant anastomotic leakage after large bowel restoration: Multivariate analysis of 707 patients. World J Surg. 2002, 26: 499-502.

12. Custem EV: Adjuvant chemotherapy of colorectal cancer. Six National Cancer Conference Oncology update, 1999.

13. Colorectal Cancer Practice Guidelines Committee: Colorectal Cancer Surgical Practice Guidelines. Oncology 1997; 11:1051-1065.

14. The Gastro-intestinal Tumor Study Group: Adjuvant therapy with hepatic irradiation plus flouorouracil in colon carcinoma. Int J Radiat Oncol Biol Phys. 1991; 21:1151-1156.

15. IMPACT Trial : Efficacy of adjuvant fluorouracil and folinic acid in colon cancer. Lancet 1995; 345:939-944.

16. Moertel CG, Fleming TR, Macdonald JS et al.: Fluorouracil plus levamisole as effective adjuvant therapy after resection of stage III colon carcinoma: a final report. Ann Intem Med 1995; 122:321-326.

17. Haller DG, Catalano PJ, Macdonald JS et al.: Fluorouracil (FU), leucocvorin (LV) and levamisole (LEV) adjuvant therapy for colon cancer: preliminary results of INT-0089. Proc Am Soc Cli Onco, 1996; 15: 211 (A486).

18. Wolmark N, Rockette H, Mamounas EP et al.: The relative efficacy of 5-FU and leucovorin (FU-LV), 5-FU + levamisole (FU-LEV) and 5-FU + Leucovorin + levamisole (FU-LV-LEV) in patients with Duke' B and C carcinoma of the colon: First report NSABP Co-4. Proc. Am Soc Clin Oncol. 1996; 15:205 (A 460).

19. 19-O'Connell MJ, Laurie JA, Kahn M et al.: Prospectively randomized trial of postoperative adjuvant chemotherapy in patients with high risk colon cancer. J Clin Oncol, 1998, 1;16:295-300.

20. Slanetz CA Jr, Herter FP and Grinnell RS: Anterior resection versus abdominoperineal resection for cancer of the rectum and rectosegmoid : An analysis of 524 cases. Am J Surg, 1972; 123:110.

21. Forloni B, Reduzzi R, Paludetti A, et al.: Intra abdominal lavage in emergency surgical treatment of left sided colonic obstruction. Dis Colon Rectum 1998; 41:23-27.

22. Basse L, Jakobsen D, Billesbolle P et al.: A clinical pathway to accelerate recovery after colonic resection. Ann Surg 2000; 232(1):51-57.

23. Tan SG, Nambiar R, Rauff A et al.: Primary rescetion and anastomosis in obstructed descending colon. Arch Surg 1991; 126 (6): 748-750.

24. Lau PW, Lo CY, and Law WL. The role of one stage surgery in acute left sided colonic obstruction. Am J Surg 1995; 169 (4):406-409.

25. Deans GT, Krukowski ZH, and Erwin ST: Malignant obstruction of the left colon. Br. J. Surg. 1994; 81 (9):1270-1276.

26. Reijnen MMPJ, DeMan BM, Postma HVA et al.: Hyaluonic acid-based agents do not affect anastemotic strength in the rat colon, in either the presence or absence of bacterial peritonitis. Br J Surg 2000; 87:1222-1228.

27. Watson AJM, Krukowski ZH, and Murno A: Salvage of large bowel anastomotic leaks. Br J Surg 1999; 86:499-500.

28. Safranek P, Bell N, and Smith JAE: Is emergency surgery a major factor influencing post-operative mortality for colorectal cancer. Br J Surg 2001; 88:27.

29. Haller DG: An overview of adjuvant therapy for colorectal cancer. Eur J Cancer 1995; 31A:1255-1263.

30. Crucitti F, Sofo, L, Doglietto GB, et al.: Prognostic factors in colorectal cancer: current status and new trends. J Surg Oncol Suppl 1991; 2:76-82.

31. Wolmark N, Rockette H, Mamounas E, et al.: Clinical trial to assess the relative efficacy of fluorouracil and leucovorin, fluorouracil and levamisole, and fluorouracil, leucovorin, and levamisole in patients with Dukes'B and C carcinoma of the colon: Results from National Surgical Adjuvant Breast and Bowel Project C-04. J. Clin Oncol, 1999; 17 (11) November :3553-3559.

32. O'Connell MJ: A phase III trial of 5-Fluorouracil and leucovorin in the treatment of advanced colorectal cancer: A Mayo Clinic /North Central Cancer Treatment Group Study. Cancer 1989; 63 (suppl 6):1026.

33. Fong Y, and Salo J: Surgical therapy of hepatic colorectal metastasis. Semin Oncol 1999; 26(5):514-523.

34. Kemeny NE; and Ron IG, Hepatic arterial chemotherapy in metastatic colorectal patients. Semin Oncol, 1999; 26 (5):524-535.