Recent Advances on the Surgical Treatment for Colorectal Cancer

December 4, 1999
International Conference Hall
Aichi Cancer Center
Nagoya, Japan
Aichi Cancer Center International Symposium VI

Recent Advances on the Surgical Treatment
for Colorectal Cancer

Committee Members

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December 4, 1999
Aichi Cancer Center, Nagoya, Japan
Program

9:45-9:50 Opening Remarks
Makoto Ogawa (Aichi Cancer Center)

9:50-11:50 Minimally Invasive Surgery
(Chairperson: K. Sugihara)

9:50-10:30
Endoscopic Treatment of Colorectal Tumor
Akira Matsuura (Aichi Cancer Center)

10:30-11:10
Laparoscopic - Assisted Colectomy for Colorectal Carcinoma
Fumio Konishi (Associate Professor, Department of Surgery, Jichi Medical School)

11:10-11:50
Laparoscopic Surgery for Rectal Cancer
Francis Seow-Choen (Clinical Associate Professor of Surgery, National University of Singapore)

11:50-13:00 Lunch

13:00-15:00 Lymphnode Dissection and Function Preserving Operation for Rectal Cancer
(Chairperson: T Mori)

13:00-13:40
The Outcome of Autonomic Nerve Preservation Operation with Lateral Dissection for Rectal Cancer
Takashi Hirai (Aichi Cancer Center)
13:40-14:20
Optimal Surgery for Rectal Cancer
Kenichi Sugihara (Professor, Second Department of Surgery, Tokyo Medical and Dental University)

14:20-15:00
Sphincter Preserving Surgery for Distal Rectal Cancer
David M. Ota (Professor of surgery, University of Missouri School of Medicine)

15:00-15:30 Coffee Break

15:30-17:30 Treatment for Recurrent Colorectal Cancer
(Chairperson: F Konishi)

15:30-16:10
Hepatic Arterial Infusion Chemotherapy for Liver Metastases from Colorectal Cancer
Yasuaki Arai (Aichi Cancer Center)

16:10-16:50
Surgical Treatment for Locally Recurrent Rectal Cancer
Takeo Mori (Tokyo Metropolitan Komagome Hospital)

16:50-17:30
Treatment of Recurrent or Metastatic Colorectal Cancer
Jin C. Kim (University of Ulsan of Medicine and Asan Medical Center)

17:30-17:35 Concluding Remarks
Suketami Tominaga (Aichi Cancer Center)
Endoscopic Treatment of Colorectal Tumor

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The endoscopic treatment has been widely performed all over the world. Recently the endoscopic mucosal resection (EMR) using submucosal saline injection technique was introduced to simplify the resection of flat or large sessile colorectal tumors.


We experienced 42 flat type colorectal carcinomas, which are 15% of total carcinoma resected endoscopically and increasing in number year by year. We had a lot of progress in detecting flat type carcinoma, which is thought to invade faster than polypoid type carcinoma into deeper layer. Ordinary polypectomy can not resect this kind of flat type carcinoma, but EMR using submucosal saline injection technique is very effective to remove it.

Endoscopic removal of sessile colorectal polyps 2 cm or greater in diameter is very difficult. EMR is recognized as a safe and effective method in these situation. However, there are several limitations in the endoscopic treatment. Carcinoma with submucosal invasion have the risk of lymph node metastasis. Additional abdominal surgery is suggested in patients with invasive carcinoma, which is to be proven after endoscopic resection. The endoscopic treatment can not cure in these patients. In our experience, 62 of 81 (76.5%) patients with the submucosal invasion were operated. 4 of 62 (6.5%) patients were proven to have lymph node metastasis. Invasion was significantly deep in all 4 patients. 19 of 81 (23.5%) patients with the submucosal invasion were followed to observe. In these 19 patients, invasion into submucosal layer was mild to moderate and there were several reason why the operation was not undertaken, such as avoiding colostomy. This limitation is from not technical but biological behavior point of view. Size has another limitation. In case it is over 3cm in diameter, it is very hard to resect completely, and so surgical operation is suggested.
We have indications and limitations in the therapy. The endoscopic treatment is not an exception. Polypectomy or EMR is an effective method to treat colorectal tumor if taking a careful consideration of indications and limitations into account.

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Major in diagnosis and treatment of gastrointestinal tumor and inflammatory bowel disease.
Laparoscopic-colectomy for colorectal carcinomas has been practiced in Japan since 1993. However, this procedure has not been widely accepted as a treatment of choice. One of the reasons for this would be the difficult technique of this procedure, and another reason is that it has not been proved that this procedure can be as curative as open colectomy as the treatment of colorectal carcinoma. In this report, we analyzed in a consecutive personal series of 131 cases in which laparoscopic colectomy were carried out from 1993 to 1999. In all the cases, the first author was the operator. The final histological diagnosis of these patients was adenoma of the colon in 8, carcinoma of the colon and rectum in 120, leiomyoma of the colon in 1 and Crohn's disease in 1 and ulcerative colitis in 1. The TNM staging of the carcinomas in our series was Tis in 10, T1 in 29, T2 in 23, T3 in 43 and T4 in 15 cases. Sites of the tumors were sigmoid in 61, right colon 30, transverse in 12, descending in 8 and rectum in 9 cases. The grade of lymphnode dissection was determined based upon the preoperative assessment of the depth of invasion. In most of the T2 and T3 cases, lymphnode dissection was carried out up to the origin of major branches of mesenteric arteries (D3). Nine of the 131 cases had to be converted to open surgery. The reasons for conversion were bleeding in 3, adhesion in 1, anastomotic problems in 2, and cancer invasion in the bladder in 1, and others. Mayor post operative complications occurred in the 9 cases in which a reoperation was carried out. These included a perforation of the colon, pancreatic fistula, ileus and bleeding. Among the 12 minor postoperative complications, a wound infection was the most frequent and occurred in 7 cases. There were no operative or postoperative deaths. The postoperative observation period ranged from 1 month to 5 years and 6 months. There were two cases with peritoneal recurrence. In these patient, no findings of port site recurrence were observed. There is another patient with high CEA level without obvious sites of recurrence. We thus consider that provided the surgeons are technically well experienced, a laparoscopic assisted colectomy is an effective and curative procedure for the treatment of colorectal carcinoma. However, in view of our complication rate,
both sufficient training and experience with the techniques are required to perform a laparoscopic colectomy are important for the future development of this procedure.

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1988- Associate Professor, Department of Surgery, Jichi Medical School
Laparoscopic Surgery for Rectal Cancer

Francis Seow-Choen

INTRODUCTION

Laparoscopic surgery for colorectal cancer remains controversial. Nonetheless, although published opinion is divided regarding laparoscopic cancer surgery, there is a widespread use of laparoscopy for colorectal cancer in practise. Good surgical techniques including strict oncological surgery and adequately radical lymphovascular and radial margins are important in maintaining a low recurrence rate and a high cure rate for colorectal cancers. A breach of these important surgical standards may be disastrously mortal. The potential benefits of laparoscopic surgery such as improved cosmesis, reduced postoperatively pain, earlier return of bowel activity and feeding, earlier functional recovery and shortened hospital stay may therefore not be important if survival is compromised. These short-term benefits must be critically balanced against the long-term recurrence and cure rates for laparoscopic colorectal cancer surgery.

CANCER SURGERY

Complete cancer excision with adequate tumour and lymph nodal clearance are essential in both open and laparoscopic cancer surgery. The recent concern that port site recurrence may be seen in up to 4.5% of cases following laparoscopic colorectal cancer surgery probably results partly from a breach of surgical oncologic principals and some from surgery in patients with advanced colorectal cancer.

LAPAROSCOPIC RECTAL SURGERY

There is no long term trial at the present time comparing the post/wound site recurrence, local recurrence or long term mortality of laparoscopic versus open rectal surgery. However the preliminary results from our prospective studies have indicated that the laparoscopic approach is safe as far as early post operative morbidity and mortality are concerned (6). Our initial experience of sixteen and eleven patients who underwent laparoscopic and open abdomino-perineal resection for low rectal cancers respectively were encouraging indeed. The median operative time was 110 mins (65 - 210) and 100 mins (80 - 185) as for laparoscopic and open techniques respectively.
There was no significant difference however in the need for post operative analgesics and time to stoma function but the laparoscopic group showed significant improvement in starting fluids, diet, ambulation and in length of hospitalization. We also studied forty consecutive patients with rectosigmoid cancers undergoing anterior resection. Twenty patients were allocated to laparoscopic and open anterior resection each. Each group was well matched in terms of Dukes’ staging. The median length of distal margin of clearance beyond the tumour was 4.0 cm (2.0 to 8.0 cm) and 4.5 cm (3.0 - 7.5 cm) in the laparoscopic and open groups respectively. Median operating time was 90 mins (55 to 185) and 73 mins (40 to 140) in the laparoscopic and open groups respectively. The length of the extraction site was 5.5 cm (4.0 to 13.0 cm) in the laparoscopic group and the wound length was 18.0 cm (8.0 to 25.0) in the open group. There was however no significant differences between the groups with regards to duration of parenteral analgesic, starting fees, time of bowel function or duration of hospitalization.

CONCLUSION

Laparoscopic rectal surgery is not difficult to perform. Short term results are encouraging as far as rectal cancer surgery is concerned.
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The Outcome of Autonomic Nerve Preservation Operation with Lateral Dissection for Rectal Cancer

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Background: we had performed lateral lymph node dissection (LLND) for rectal cancer since 1975. Although the efficacy of lateral lymph node dissection in lower rectum was proved by historical comparative study, the urinary and sexual dysfunction frequently occurred after operation. Therefore we have started autonomic nerve preservation operation with LLND since 1987. The aim of this study was to evaluate the oncological outcome and functional results of the procedure.

Methods: From 1987 to 1997, 153 upper and lower rectal cancers were treated with autonomic nerve preservation operation with LLND, 83 by total nerve preservation and 70 by partial nerve preservation. LLND is applied for T2 tumor and the deeper tumor than T2 in lower rectum and anal canal and for T3 tumor and the deeper tumor than T3 in upper rectum. Among LLLD total nerve preservation was indicated for the tumor which showed no lymph node metastasis in the mesorectum by intraoperative pathological examination. If lymph node metastasis was proved, partial nerve preservation was adopted. Location of the tumor was upper rectum in 41 patients, lower rectum in 118 and anal canal in 4. According to Dukes’ classification, A 46 patients, B 33 patients, C 74 patients, respectively.

Results: Frequency of voiding dysfunction which means need of self-catheterization at the discharge among patients with total nerve preservation was 1 of 83 patients (1 per cent) and with partial nerve preservation 5 of 70 patients (7%). After total nerve preservation LLND, frequency of male sexual dysfunction on inquiry was 8 of 22 patients (36 per cent) for erectile dysfunction and 17 of 22 patients (77 per cent) for ejaculatory dysfunction. The local recurrence rate with total nerve preservation was 2 of 83 (2%), and with partial nerves preservation 9 of 70 (13%). The overall 5-year survival rate after total nerve preservation was Dukes’ A 93 per cent, Dukes’ B 88 per cent, Dukes’ C 72 per cent and after partial nerve preservation was Dukes’ A 100 per cent, Dukes’ B 75 per cent, Dukes’ C 70 per cent.

Conclusion: Autonomic nerve preservation operation with LLND for rectal cancer was
performed without compromising the chance of cure. Preservation of voiding function was acceptable. Erectile function was preserved well but ejaculatory function was injured at a high rate even if autonomic nerve supposed to be spared completely.
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Special courses & experience:
Surgical treatment of colorectal cancer
Optimal Surgery for Rectal Cancer

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Surgical treatment of rectal cancer still has serious problems both in local control and quality of life after surgery: high local recurrence rate with 11 % to 30%, loss of the anal sphincter, disturbance of defecation and urinary and sexual dysfunction. These serious problems may come from two anatomical conditions. First, there are two pathway of lymphatic drainage of the low rectum: superior lymphatic drainage which courses along the superior rectal vessels to the origin of the inferior mesenteric artery and lateral lymphatic drainage which occurs along the middle rectal artery in the lateral ligament, via the internal and common iliac nodes to the paraaortic nodes. Second, genitourinary organs are located adjacent to the rectum and the autonomic nerves supplying these organs run along the rectum.

In order to achieve local control, extended pelvic lymph node dissection (EPND), preoperative (chemo-)radiotherapy and total mesorectal excision (TME) has been introduced. EPND has changed to EPND with pelvic autonomic nerve preservation (PANP) because of high frequency of severe autonomic dysfunction after surgery. A basic standard procedure of resection of the rectum is anatomically to mobilize the rectum which is enveloped with the rectal fascia both from the surrounding organs (the pelvic wall including the iliac vessel system, the seminal vesicles, the prostate, the vagina and the sacrum) and from the pelvic autonomic nerve system which locates on the rectal fascia. This can be called complete circumferential mesorectal excision (CCME). Therefore, EPND with PANP means CCME combined with pelvic side wall dissection (PSWD) which aims to eradicate lateral lymphatic drainage, and TME means CCME combined with complete removal of the distal mesorectum down to the pubo-rectal muscle (CDME) which intend to remove all cancer deposits spreading anally in the mesorectum.

The problem is whether addition of PSWD or CDME to CCME is of benefit to control local recurrence and to improve the prognosis. Many studies in Japan reported that lateral lymph node metastases from rectal carcinoma located at or below the peritoneal reflexion was approximately 15% and the 5 year survival rate of patients...
with positive lateral lymph node ranged from 12% to 40%, consequently 2% to 6% of patients benefit from PSWD. PSWD may be effective for quite a small subgroup of rectal cancers and patients selection for PSWD is important to increase its effectiveness. The prospective study which investigated cancer spread in the bowel wall and the mesorectum in consecutive 38 rectal cancers disclosed that 16% showed anal cancer spread and the longest distance of cancer spread in low rectal cancer was 11 mm. This study may indicate CDME is not necessary, but complete removal of the mesorectum to the distal resection line (not to make core shape resection of the mesorectum) is important.

Type of surgery for rectal cancer should be adopted individually according to preoperative cancer staging in consideration of its effectiveness on local control.
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1987 - 1989: Surgeon, Dept. Surgery 1, Tokyo
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1997 - present: Professor, Second Department of Surgery, Tokyo Medical and Dental University
Sphincter Preserving Surgery for Distal Rectal Cancer

David M. Ota

Objectives:

1. To understand the role of local excision of rectal cancers

2. To understand organ preservation for rectal cancer

Background:

There have considerable advances in the treatment of colorectal cancer. Large scale national trials have been conducted and new investigations have started. Because surgery has an important role in the treatment of colorectal cancer, an awareness of new surgical techniques is important to patients with this disease. Local excision of early rectal cancer and sphincter preserving surgery for distal rectal cancer are important management issues to avoid an abdomino-perineal resection and permanent colostomy. Local excision of early rectal cancer has become an important topic for sphincter preservation. This is an extension of local excision therapy for early breast cancer followed by postoperative radiation therapy. The hypothesis is that if early rectal cancers are locally excised and radiated, local control of disease is as successful as breast conversation surgery followed by radiation therapy. A national trial was conducted to test this hypothesis in a phase II single arm study(1). One hundred ten patients had complete local excision of their T1 or T2 rectal cancers. Patient eligibility criteria included histologic assessment of tumor free margins and depth of invasion into the bowel wall. T3 rectal cancers were excluded from this study. T1 cancers underwent surgery alone and T2 cancers underwent local excision followed by postoperative pelvic radiation therapy. At a median follow up of four and a half years, the local recurrence rate for T1 rectal cancer was 7%. The local recurrence rate for T2 cancers was 18%. All patients underwent successful salvage abdominal perinea[ resection. The conclusion is that further investigations are necessary. A local recurrence rate of 18% is significant for T2 disease that is treated successfully with sphincter-preserving proctectomy. Further studies are necessary in order to evaluate
Sphincter preservation for rectal cancer is a highly desirable goal. A recent study was done in 680 patients from many hospitals from the upper Midwest participating in an NCI cooperative group trial (2). Six hundred eighty rectal cancer patients were evaluated and the incidence of abdominal perineal resection was 45%. In this study, the distal margin length was not a factor in predicting local recurrence. Sixteen percent of the 680 patients had a distal margin of less than 1 cm. This brings up an important topic of how much distal margin is necessary and this study challenges the surgical dictum that an abdomino-perineal resection is necessary to achieve a 2 cm distal margin. The role of preoperative therapy for rectal cancer is still being investigated. At the Ellis Fischel Cancer Center patients with rectal cancer (<12 cm from the anal verge) have received preoperative therapy as part of a strategy to reduce tumor size and avoid an abdomino-perineal resection. Considerable shrinkage of tumor is achieved with preoperative chemoradiation therapy such that many patients with distal rectal cancers are eligible for sphincter preserving procedures that remove the sigmoid and rectum with ultra low coloanal anastomoses. Sphincter function is preserved and continence is achieved in approximately 95% of the patients. In the Ellis Fischel series our data show that the distal margin length is not a significant determinant of local disease control and survival. Problems associated with low anastomoses include stool frequency, clustering of bowel movements, and irregularity of bowel movements. Our data suggest that sphincter preserving surgery can be done for 95% of patients with rectal cancer. Rectal adenocarcinoma responds significantly to preoperative chemoradiation therapy which is crucial for increasing sphincter preservation.
References


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Clinical Areas of Special Interest:
Breast and Colorectal Neoplasms and Minimal Invasive Surgery in Cancer Management
Hepatic Arterial Infusion Chemotherapy for Liver Metastases from Colorectal Cancer

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Hepatic arterial infusion chemotherapy is standing on the adequate drug distribution to the Liver. However, this therapy has been evaluated for long time by clinical trials without technical considerations. The techniques for this therapy have been completely changed in the last decade by the advances of interventional radiology. The hepatic arterial catheter and port system can be placed percutaneously under local anesthesia using interventional techniques, and the drug distribution can be evaluated and managed using CT angiography.

For liver metastases from colorectal cancer, so called WHF (Weekly High dose 5FU) regimen (5FU 100mg/m2/5hour qw) has been developed and commonly used for hepatic arterial infusion in Japan. Hepatic arterial infusion chemotherapy using WHF regimen can be performed out-hospital bases without major toxic events. In a phase 11 study of WHF regimen for 30 patients (pts) with unresectable liver metastases and without extra-hepatic lesions, the response rate (RR), the median survival (MS) and the prevention rate of hepatic death was 83%, 26months (mos) and 76%, respectively. On the other hand, in a multi-institutional study (JHAISG) for 199 patients with unresectable liver metastases, RR and MS was 52% and 16 mos, respectively, and MS of pts with no or controlled extra-hepatic lesions was significantly longer compared with that of pts with progressive extra-hepatic lesions (21mos vs 11mos).

These results suggest that using interventional techniques we can control liver metastases under minimally invasion without the reduction of pts' QOL. Thus, hepatic arterial infusion chemotherapy should be reappraised by studies using interventional techniques, and the combination with systemic chemotherapy must be discussed for the longer survival.
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Arterial infusion chemotherapy
Interventional radiology
Surgical Treatment for Locally Recurrent Rectal Cancer

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The most difficult problem to treat surgically for locally recurrent rectal cancer is to get the safety surgical margin. Always recurrent tumor is covered with thick fibrotic hard operation scar of previous operation. Intra-operative judgement of the area where the cancer cells are invaded is so much difficult that it is often to make excessive operation such as total pelvic exenteration. Although the resection is too much stress for the patients, surgical resection is the most effective concerning with the survived period of the patients, and with the regressing the complaints of them such as severe pain and repeated urinary infection. The result of surgical resection was not so much successful that 5 years survival rate of all cases was only 21%. But to make careful analysis was given us some hopeful data. Those who could get the macroscopically free surgical margin survived longer than couldn't it with statistically significant difference. Of course patients received complete resection proved microscopically were survived longer, but it was not significant the difference between macroscopically negative surgical margin but microscopically positive group and microscopically negative group. According to these results, we started to make curative high dose of preoperative radiation such as 70Gy, and combined with mutimodal treatment to get the free surgical margin. Though the operation itself became more difficult one, the local control rate was apparently improved respectively. Moreover, the result of decreasing tumor size allowed a little of space to save the function of patients for example preserving anal function or nerve, making reconstructed urinary bladder. We will speak about such result and the future view of multimodal treatment for locally recurrent cancer.
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Treatment of Recurrent or Metastatic Colorectal Cancer

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The recurrent and metastatic colorectal cancers used to be used in a single terminology, revealing colorectal cancer cells other than primary lesion. In a strict sense, the recurrence means a recrudescence of the primary lesion after curative surgery regardless of its location. Although more than two-thirds of patients are candidates for curative surgery, recurrence is as many as 40% after curative resection. As most of the recurrence occurs within two years after surgery, they come from neglected or unidentified tumor at the initial surgery. Treatment modalities of recurrent or metastatic tumors depend on extent, multiplicity, location of tumors, and physical status of patients. They include all forms of surgery, chemotherapy, irradiation, and other sophisticated tools that can be used as curative or palliative purpose. As recognized in the primary colorectal cancer, surgery is the most promising to cure if performed in an adequate time. Fortunately, recent diagnostic tools, e.g., CT, MRI, endosonography, and PET, in addition to classical serial measurement of serum carcinoembryonic antigen (CEA) and colonofiberscopy enable early and accurate detection of recurrence or metastasis. Consequently, more than one third of them have a chance for curative surgery and other one third for more efficient tools expecting prolongation of survival and enhancing quality of life (QOL). The common sites of recurrences are loco-regional, liver, lung, other intra-abdominal viscera, bone, and brain in descending order of frequency. The curative surgery rate for the first three sites is around 25 to 40% with similar rate of 5-year survival. Single or localized recurrence and metastasis in the other intra-abdominal viscera or brain can be also cured by surgery. However, they appear to include other frequent sites of metastasis as well at the time of tumor detection by targeting the gamma emission from tumor cells attached to radiolabeled antibodies. Although accurate identification of small foci, not identified in ordinary surgery, may be possible in recurrent or metastatic tumors, RIGS includes several problems to be solved until now. One is limited expression of tumor antigen including TAG-72 and CEA, and the other is false-positive detection of tumor cells. Chemotherapy can be applied either systemically or regionally regarding
the location. Hepatic arterial infusion chemotherapy has been most widely performed for the liver metastasis with it showing several promising results: unresectable, adjuvant purpose after resection of multiple metastases, reducing the size or number before resection. Intraperitoneal chemotherapy is the other form of regional chemotherapy for the pelvic or intraperitoneal recurrences. Technique of hyperthermia was also combined with various results. In case of intractability to ordinary regimen of 5-FU and leucovorin, a new form of platinum (oxaliplatin) and other thymidylate synthase (ratritrexed) may be another choice in their initial phase trials. Radiotherapy can be an efficient local treatment for both curative and palliative intent. Intraoperative radiotherapy and brachytherapy can be helpful in the residual or inaccessible tumors. Localized irradiation to bone metastasis may alleviate severe back pain in the vertebral metastasis. In conclusion, a standard treatment of recurrent or metastatic colorectal cancer cannot be easily definable considering its diverse presentation. Even a treatment modality enabling a little prolongation of survival or increment of QOL must be evaluated for the conquest of these troublesome situations.
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