ORIGINAL ARTICLE

Clinical outcome of open and laparoscopic surgery in Dukes' B and C rectal cancer: experience from a regional hospital in Hong Kong

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Objective To compare the long-term outcome of open and laparoscopic surgery for Dukes' B and C rectal cancer in a regional hospital in Hong Kong.

Design Retrospective study.

Setting A regional hospital in Hong Kong.

Main outcome measures Survival and local recurrence rates.

Patients Patients with Dukes' B and C rectal cancers underwent elective curative open or laparoscopic surgery during the period December 2000 to December 2006.

Results A total of 222 patients (open surgery, n=133; laparoscopic surgery, n=89) were assessed. The overall 3- and 5-year survival rates for all patients were 72% and 58%, respectively. Local recurrence rates were similar in both groups. Laparoscopic group had better overall survival (P=0.014), however. The overall 3-year survival rates were 79% and 68% in the laparoscopic and open groups, respectively. The corresponding 5-year rates were 75% and 52%. Multivariate analysis also demonstrated that laparoscopic surgery was a significant independent factor for better survival. Chemotherapy, local recurrence, lymph node metastasis, and poorly differentiated tumour were significantly associated with survival.

Conclusion Laparoscopic surgery for Dukes' B and C rectal cancer was associated with more favourable survival than with open surgery.

Introduction

Colorectal cancer is one of the most common cancers in the world. According to the Hong Kong Cancer Registry by Hospital Authority, there were 4084 new cases diagnosed in 2007 and the trend is increasing.[1] Concerning the management, surgical resection is the primary treatment. With the advances in technology and technique, laparoscopic surgery is now commonly performed for colorectal cancer.

Laparoscopic colorectal surgery was reported in 1991.[2] However, in the beginning there were great concerns about the port-site recurrence, cost-effectiveness, demanding surgical skill, and oncological clearance.[3-5] The advantages of laparoscopic colorectal surgery were not recognised until some authors began to report the feasibility and favourable short-term outcomes including faster recovery of bowel motility, shorter hospital stays, and less stress.[6-8]

Rectal cancer surgery is a challenge to colorectal surgeons, due to the narrow and limited operative field. However, laparoscopic surgery provides potential benefits, namely: better visualisation from the laparoscopic camera and precise tissue handling by laparoscopic instruments. We believed that the advantages of laparoscopic surgery might improve clinical outcomes in patients surviving rectal cancer, and encouraging results were also described in several specialised centres.[9,10]

The aim of this study was to compare the long-term outcome of laparoscopic and open surgery in patients with Dukes' B and C rectal cancer in Kwong Wah Hospital, a regional hospital in Hong Kong.

Key words
Disease-free survival; Laparoscopy; Neoplasm recurrence, local; Rectal neoplasms; Treatment outcome

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Methods

In the Department of Surgery in our hospital, laparoscopic surgery for rectal cancers was introduced in the late 1990s. However, until 2007 its application was limited to rectal cancer. During the period between 2000 and 2006, the rate of laparoscopic operations for rectal cancers ranged from 12.5 to 50%. There were two separate groups of surgeon specialists with similar experience in colorectal surgery, one group performed open surgery, and during the same period another group performed laparoscopic surgery. Selection of the operative approach depended on patient's choice and surgeon's preference. Same management protocol was applied to all patients except for the operative approach.

Patients

During the period December 2000 to December 2006, all patients with Dukes' B and C rectal cancers having elective curative resection in Kwong Wah Hospital were included in this retrospective study.

Preoperative preparation

Before the operation, colonoscopy was performed on all eligible patients. Barium enema or computed tomography (CT) was arranged for tumour localisation in cases having incomplete colonoscopy or unclear colonoscopy finding. Preoperative staging was assessed by chest X-ray, abdominal ultrasound, and CT or positron emission tomography (PET) scans. Routine bowel preparation with 2 to 4 L polyethylene glycol was prescribed. A second-generation cephalosporin and metronidazole were given on induction of general anaesthesia.

Surgical procedure

Lower midline incisions were performed for all open operations. The five-port technique was used for laparoscopic operations; ports being inserted at the subumbilical region (12 mm), right upper quadrant (5 mm), right lower quadrant (12 mm), left upper quadrant (5 mm), and left lower quadrant (12 mm). The lateral-to-medial approach was adopted in both groups. High or low ligation of the inferior mesenteric artery was based on the surgeon's preference. Total mesenteric excision was performed in all cases. Specimens were retrieved via the extended left lower quadrant wound in the laparoscopic group after intracorporeal distal transection. Anastomoses were achieved by double stapling. Coloanal anastomoses were also performed in ultra-low anterior resections. Diversion ileostomy was routinely performed in low anterior resections.

傳統開腹手術及腹腔鏡手術在杜克斯B期及C期直腸癌的臨床結果：香港一間分區醫院的經驗

目的 比較傳統開腹手術及腹腔鏡手術在杜克斯（Dukes'）B期及C期直腸癌應用上的臨床結果。

設計 回顧性研究。

安排 香港一間分區醫院。

主要結果測量 存活率及局部復發率。

參與者 2000年12月至2006年12月期間，接受傳統開腹手術或腹腔鏡手術的杜克斯B期及C期直腸癌患者。

結果 共評估了222位患者的臨床結果，其中包括133位接受傳統開腹手術及89位接受腹腔鏡手術的病人。三年和五年總存活率分別為72%及58%。兩組患者的局部復發率相似，但接受腹腔鏡手術的病人有較佳總存活率（P=0.014）。接受腹腔鏡手術及傳統開腹手術的病人，三年總存活率分別為79%及68%，而五年總存活率則分別為75%及52%。多因素回歸分析亦顯示腹腔鏡手術是改善存活率的獨立重要因素。其他重要因素包括化療、局部復發、淋巴結轉移和分化不良的癌細胞。

結論 在杜克斯B期及C期直腸癌的治療中，腹腔鏡手術相對傳統開腹手術有較佳存活率。

Postoperative period

Diet was resumed on postoperative day 3 or 4. Intensive care unit care was provided for patients with poor co-morbidity and unstable intra-operative conditions. Patients were discharged from hospital or transferred to a rehabilitation hospital when the surgical condition was stable. Decisions about adjuvant chemotherapy for each individual were made collectively by the surgeons, the patients, and the oncologists.

Follow-up evaluation

The follow-up interval was every 3 months in the first 2 years, and every 6 months in subsequent 3 years. Follow-up assessment was based on the medical history, physical examination, endoscopy, and the results of imaging. Ultrasounds were performed every 6 months. Surveillance colonoscopy was performed 1 year and 4 years after the operation. Other imaging studies (chest X-rays, CT and PET scans) were arranged in cases of suspected local or systemic recurrence. Local recurrence was defined as the presence of disease in the pelvic cavity revealed by imaging or histology. Re-operations for local recurrences were performed only in certain cases.

Data analysis

All data were retrieved from the prospective colorectal database in our department. The Statistical Package for the Social Sciences (Windows version 15; SPSS Inc, Chicago [IL], US) was used for data analysis. Chi squared or Fisher's exact tests were used to compare categorical variables. The Mann-Whitney *U* test was used to compare median values of continuous variables. Survival and local recurrence rates were calculated using the Kaplan-Meier method, comparisons being made using the log-rank test. Cox regression analysis was used in determining hazard ratios of different factors in the univariate and multivariate analyses.

TABLE 1. Demographics and clinical outcomes in patients having laparoscopic and open surgery

Characteristics	Laparoscopic (n=89)	Open (n=133)	P value
Male	65 (73%)	82 (62%)	0.079
Age (years)	66.4	66.7	0.876
ASA*			0.867
1	24 (27%)	38 (29%)	
2	50 (56%)	70 (53%)	
3	15 (17%)	25 (19%)	
Stage			0.704
IIA	35 (39%)	51 (38%)	
IIB	5 (6%)	8 (6%)	
IIIA	5 (6%)	5 (4%)	
IIIB	24 (27%)	29 (22%)	
IIIC	20 (22%)	40 (30%)	
Lymph node +ve	48 (54%)	72 (54%)	0.976
Tumour level			0.01
Upper (10.1-15 cm)	22 (25%)	45 (34%)	
Mid (5.1-10 cm)	30 (34%)	58 (44%)	
Lower (0-5 cm)	37 (42%)	30 (23%)	
Lymphovascular permeation +ve	16 (18%)	23 (17%)	0.896
Perineural invasion +ve	12 (13%)	11 (8%)	0.212
Types of operation			0.094
Abdominoperineal resection	28 (31%)	26 (20%)	
Low anterior resection	37 (42%)	61 (46%)	
Anterior resection	21 (24%)	33 (25%)	
Hartmann's operation	3 (3%)	13 (10%)	
Complications	14 (16%)	19 (14%)	0.767
Re-operation	4 (4%)	9 (7%)	0.104
30-Day mortality	0 (0%)	2 (2%)	0.371
Blood loss (mL)	335.4	302.5	0.342
Median (range) hospital stay (days)	9 (5-15)	11 (7-20)	0.274
Adjuvant chemotherapy	46 (52%)	72 (54%)	0.900
Radiation therapy	8 (9%)	16 (12%)	0.517
Local recurrence	7 (8%)	9 (7%)	0.756
Systemic recurrence	28 (31%)	38 (29%)	0.369

* ASA denotes American Society of Anesthesiologists

Results

A total of 379 patients with rectal cancer were operated on during the period between December 2000 and December 2006. After excluding the emergency operations (n=36), patients with Dukes' A rectal cancer (n=102), and patients underwent palliative resection (n=19), there were 133 open operations and 89 laparoscopic operations. In all, laparoscopic surgery in 26 (29%) of the patients had the operation converted to an open procedure due to bulky tumour (n=14), severe adhesions (n=6), bleeding (n=4), and stapling failure (n=2).

The mean age of the patients was 67 years; 147 (66%) were males. The median follow-up of surviving patients was 37 (range, 1-79) months in the laparoscopic group and 38 (range, 1-102) months in the open group (P=0.437). Overall 3- and 5-year survival rates were 72% and 58%, respectively.

Comparison of demographics and clinical outcomes in the two groups is shown in Table 1. Patients in both groups were similar except there were more patients with lower rectal cancers in the laparoscopic group. The study in this period did not show additional short-term benefit in terms of complications, re-operation, hospital stay, blood loss, and 30-day mortality.

The proportion of cases with local recurrence

TABLE 2. Univariate analysis of potential factors for disease-free survival

Factor	Hazard ratio (95% confidence interval)	P value
Male	0.92 (0.60-1.58)	0.923
Lymph node +ve	2.55 (1.54-4.21)	<0.001
Poorly differentiated tumour	2.20 (1.35-3.57)	0.002
Age >70 years	1.39 (0.86-2.23)	0.179
Laparoscopic approach	0.60 (0.37-0.99)	0.045
Complications	0.84 (0.47-1.50)	0.550
ASA* ≥3	1.13 (0.61-2.09)	0.694
Lymphovascular permeation	1.67 (0.99-2.84)	0.049
Perineural invasion	1.78 (0.88-3.61)	0.108
Level of tumour (lower)	0.88 (0.47-1.63)	0.678
Radiation	1.60 (0.82-3.12)	0.168
Chemotherapy	0.39 (0.24-0.65)	<0.001

* ASA denotes American Society of Anesthesiologists

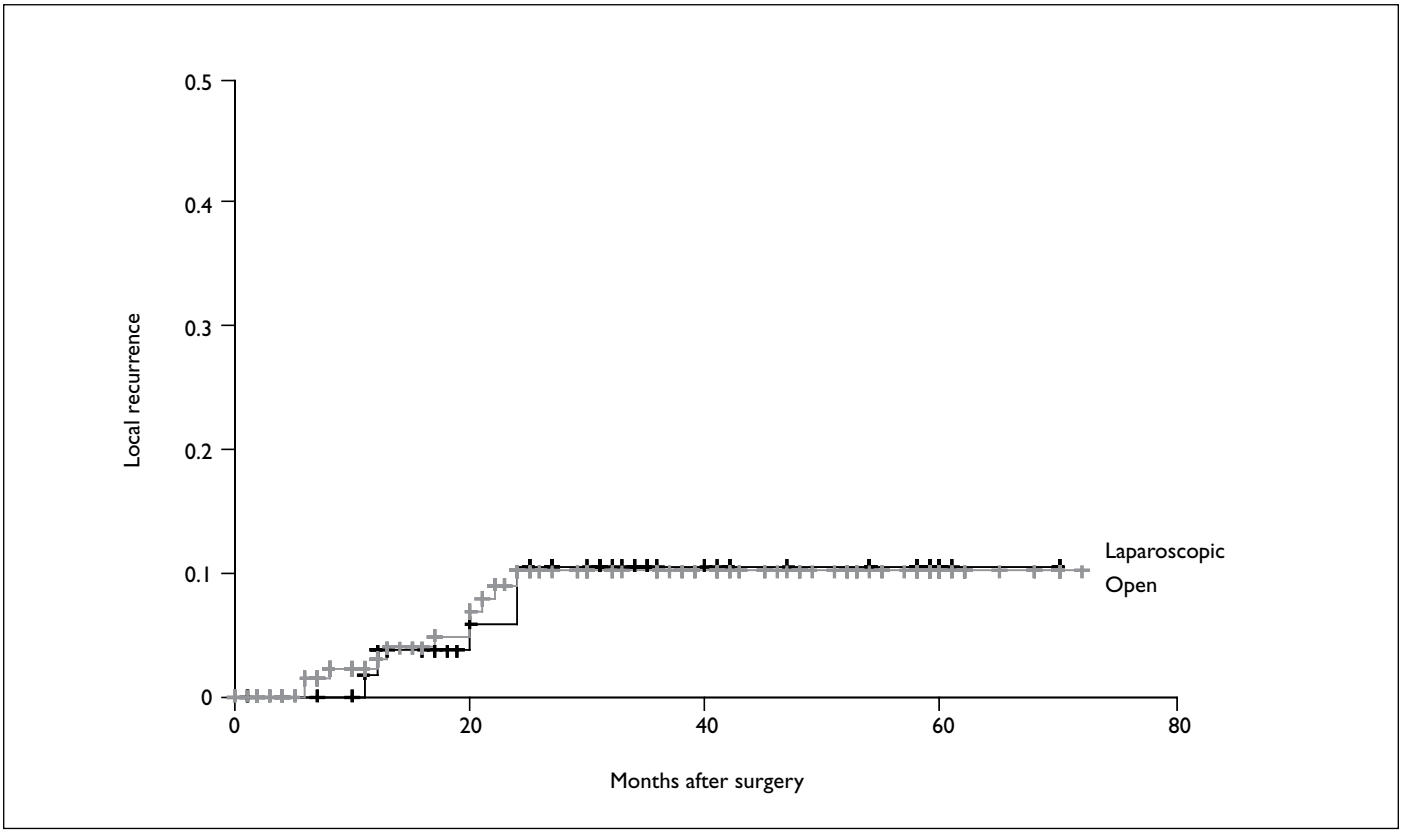

FIG 1. Comparison of local recurrence rates after laparoscopic and open surgery (P=0.994)

was similar (P=0.756) in both groups (Fig 1), 7 (8%) laparoscopic versus 9 (7%) open. The mean times to local recurrence were 12 and 17 months, respectively (P=0.734).

The results of univariate analysis of potential factors related to disease-free survival (DFS) are shown in Table 2. Multivariate analysis showed that factors associated with a poor prognosis included: lymph node metastasis, poorly differentiated carcinoma, and lymphovascular permeation. The laparoscopic approach and chemotherapy were independent significant positive factors for overall survival in patients with Dukes' B and C rectal cancers (Table 3).

TABLE 3. Multivariate analysis of factors affecting disease-free survival

Factor	Hazard ratio (95% confidence interval)	P value
Lymph node +ve	2.36 (1.42-3.91)	0.001
Poorly differentiated tumour	2.14 (1.30-3.51)	0.003
Laparoscopic surgery	0.60 (0.37-0.99)	0.045
Lymphovascular permeation	1.84 (1.10-3.08)	0.020
Chemotherapy	0.44 (0.33-0.85)	0.002

The comparison of overall survival in the laparoscopic and open groups is shown in Figure 2. It reveals better overall survival in the laparoscopic group (P=0.014); 3-year overall survival rates were 79% and 68% in laparoscopic and open groups, respectively, and the corresponding figures for 5-year overall survival were 75% and 52%.

A significant difference in DFS between the groups is illustrated in Figure 3 (P=0.021). The 3-year DFS was 79% and 66% in the laparoscopic and open groups, respectively; the corresponding figures for 5-year DFS were 62% and 50%.

Discussion

Several randomised controlled trials have been performed to compare outcomes of laparoscopic and open operations for colon cancer.[11-13] They showed better short-term outcomes after laparoscopic surgery but no difference in the overall survival and recurrence, except that Lacy et al[11] reported a survival benefit after laparoscopic procedures in the stage III colon cancer. All these trials, however, only focused on disease in colon, not in rectum.

The MRC CLASICC[14] study included patients with rectal cancer and it did not demonstrate any statistically significant advantage for laparoscopic

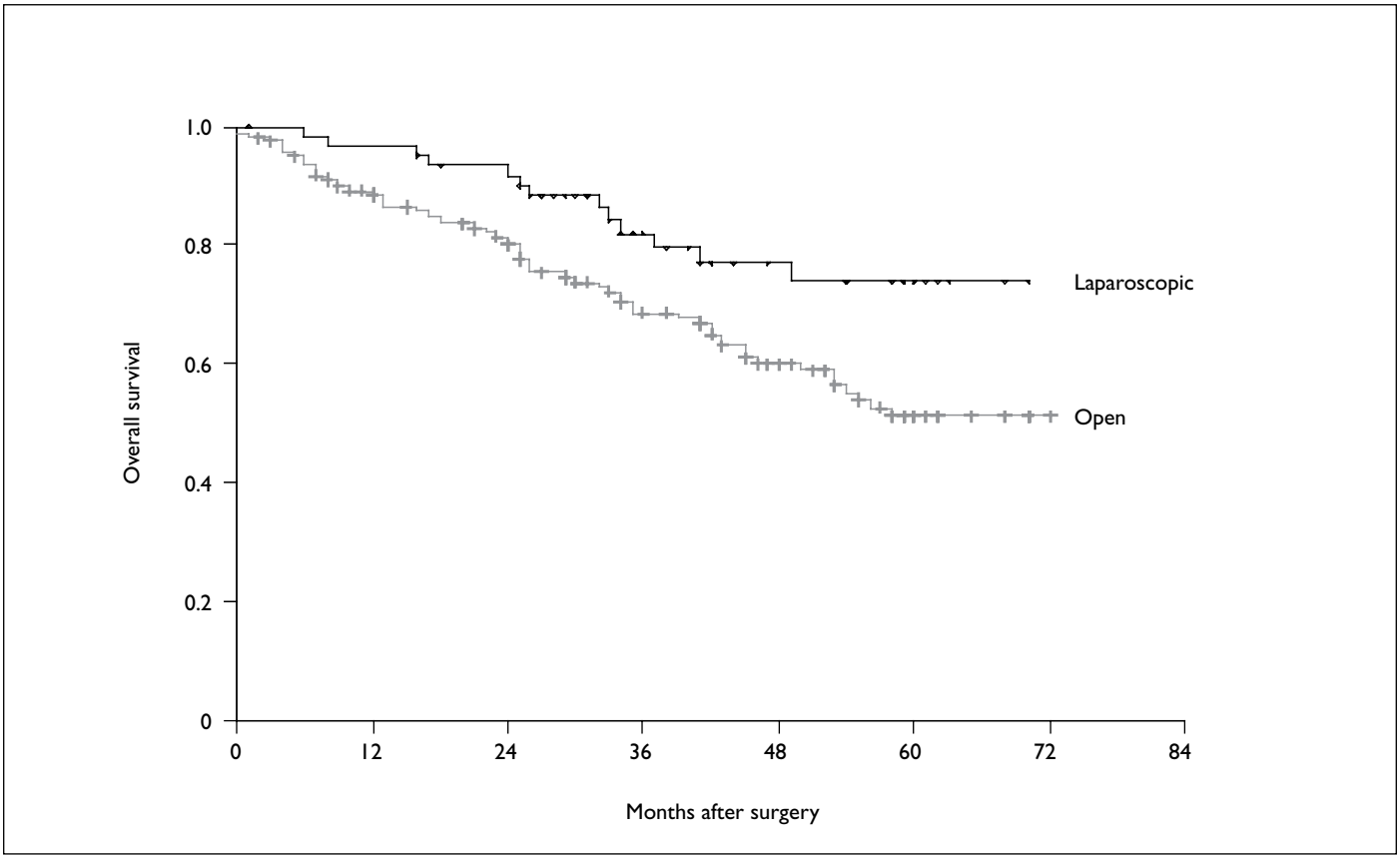

FIG 2. Comparison of overall patient survival after open and laparoscopic surgery (P=0.014)

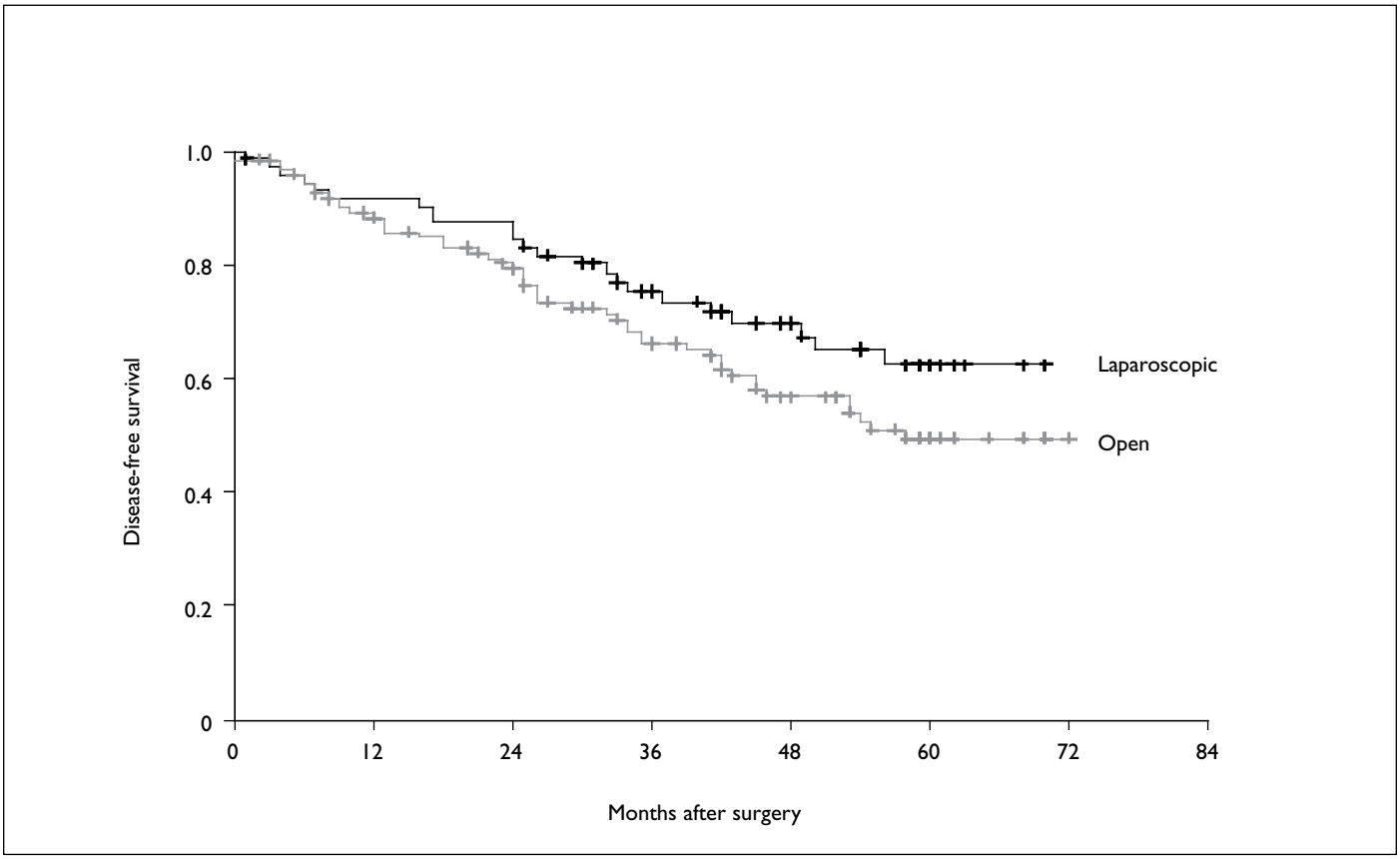

FIG 3. Comparison of disease-free survival in patients after open and laparoscopic surgery (P=0.021)

surgery, though a non-significant trend for improved 3-year overall survival was observed in Dukes' A rectal cancers. However, application of this technique to treat rectal cancer was being challenged because their favourable results depended on subgroup analysis, and relevant sample sizes and power calculations were not detailed in their study.[15] In addition, there was a high conversion rate (38%) in those undergoing laparoscopic surgery during the initial phase of the trial.

Two randomised controlled trials were conducted by Ng et al[16,17] to compare laparoscopic and open surgery for patients with upper and lower rectal cancers. The study on upper rectal cancer (n=153) entailed a subgroup analysis of a formerly conducted randomised trial on laparoscopic colorectal cancer. Although the study showed no significant difference (P=0.595) in overall survival, the laparoscopic group (84%) faired slightly better than the open group (78%).[16] The other study by Ng et al[17] on lower rectal cancers (n=99) focused on result after abdominoperineal resection, and showed no survival benefit for laparoscopic surgery. However, most of the rectal cancers were located in the mid-rectum and these two trials did not address that issue.

We believe that the advantage of laparoscopic surgery is more obvious in the advanced disease. Although seldom mentioned, studies by Lacy et al[11] and Law et al[18] showed better survival after laparoscopic colectomy and rectal resection for stage III disease, respectively. The reason is uncertain, but it could be due to better visualisation and more precise dissection using laparoscopy, which presumably results in better oncological clearance and improved immunologic responses. Our study also demonstrated better overall survival and DFS rates for Dukes' B and C rectal cancer in the laparoscopic group.

The limitations of our study were that it was retrospective, such that selection bias becomes one of the most important and unavoidable drawbacks. Common sense would indicate that more upper rectal cancers are more amenable to laparoscopic surgery, as anterior resections required for this tumour location are expected to be easier and less time-consuming. Surprisingly, in our study there were more cases of lower rectal cancers in the laparoscopic group, despite the greater technical difficulties presented by rectal tumours in this location. Therefore, we do not consider that the greater proportion of lower rectal cancers in the laparoscopic group indicates the beneficial effect on survival is false.

Local recurrence rate is an important index of surgical technique for the performance of tumour and lymph node clearance in rectal cancer surgery. Poor surgical skill may be associated with higher local recurrent rates, but we did not encounter a significant difference in the open and laparoscopic groups (Fig 1). Although it may not be possible to draw any conclusions about the skills and experience of both groups of surgeons, their surgical competence was considered to be quite similar.

As in the MRC CLASICC trial,[14] in our study the overall high conversion rate in the laparoscopic surgery group (29%) revealed the learning curve problem. Fortunately, the conversion rate decreased to 19% in the last year of the study period, and in the last 2 years it was only 10% (unpublished data). Despite the learning curve effect, survival in the laparoscopic group was superior to that in the open group. Moreover, the multivariate analysis demonstrated that the laparoscopic approach was an independent significant factor associated with a better survival.

As of now, the benefit of laparoscopic operation for rectal cancer for long-term survival remains controversial. We hope that the multicentre COLOR II trial,[19] which was conducted in 27 hospitals, can provide an answer in the near future. In addition, the Japanese multicentre randomised trial comparing laparoscopic and open colorectal operations finished registration of patients in March 2009.[20] The latter is an interesting study which includes only advanced cancers (T3, T4), and D3 lymphadenectomy is performed in both arms; it embraces the Japanese classification of colorectal carcinoma,[21] and may provide new insights about the surgical management of the advanced rectal cancer.

In conclusion, our study showed that the laparoscopic surgery for Dukes' B and C rectal cancer is associated with more favourable survival rates compared with open surgery.

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