

Original Article

Long-term Outcome of Colectomy for T1 Colon Cancer after Endoscopic Polypectomy

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Key Words

pT1 colon cancer;
Radical colectomy;
Limited colectomy

Purpose. This study aimed to compare the long-term outcomes between radical and limited colectomy for patients with pT1 colon cancer after endoscopic resection.

Methods. The clinical data of patients who underwent colectomy for pT1 colon cancer after endoscopic polypectomy from January 2000 to December 2010 were reviewed from a prospectively constructed database. Clinico-pathological features and oncological outcomes were compared between radical colectomy and limited colectomy groups.

Results. A total of 68 patients were included in this study. Twenty-seven patients underwent limited colectomy and 41 underwent radical colectomy. The latter group had more harvested lymph nodes (10.7 ± 6.9 vs. 7.3 ± 5.4 , $p = 0.034$), while the former group had a higher lymph node metastatic rate (11.1% vs. 0.0%, $p = 0.029$). The recurrence rate (3.7% vs. 0.0%, $p = 0.214$) and overall (95.5% vs. 97.5%, $p = 0.373$) and disease-free survival (95.5% vs. 97.5%, $p = 0.354$) did not differ significantly between the groups. No surgery-related deaths occurred, and the rate of surgical complications did not differ between the groups; however, the presence of complications was an independent prognostic factor for poor disease-free survival.

Conclusions. Although the lymph node metastatic rate was higher in the limited colectomy group, the oncological outcome in terms of recurrence rate and overall and disease-free survival did not differ between radical and limited colectomy for pT1 colon cancer after endoscopic polypectomy. Additionally, there was no difference in surgical morbidity and mortality between the groups.

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Colorectal cancer (CRC) is an important cause of morbidity and mortality throughout the world. It accounts for over 9% of the total cancer incidence and

is the third most common cancer worldwide and the fourth most common cause of death.¹ The 5-year survival rate of CRC has been reported to range from

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93% in stage I to 75-95% in stage II and 44-83% in stage III.^{2,3} Because of the national policy for cancer screening in Taiwan, the number of CRC cases detected early has increased in recent years.³ The traditional standard treatment for early CRC has been challenged because of the benefits of less invasive treatment modalities, such as endoscopic mucosal/submucosal dissection and transanal microsurgery. However, studies have reported high rates of local recurrence after these treatments.⁴⁻⁶ Recurrence is related to residual disease or metastasis in regional lymph nodes, and the risk of CRC spreading to the lymph nodes is between 0% and 12% in T1 patients.⁷ Thus, the National Comprehensive Cancer Network (NCCN) recommends colectomy in high-risk pT1 CRC after endoscopic resection.

The prognosis is generally good after radical resection for early CRC, with a recurrence rate of 1.3%.⁸ Nonetheless, standard colectomy, whether conducted with laparoscopic assistance or as open surgery, is associated with significant morbidity and mortality.⁹ Therefore, a less invasive resection has been used in some cases. In the present study, we evaluated the results of limited versus radical colectomy for early CRC (pT1) after endoscopic resection to determine whether both procedures yielded equivalent short- and long-term outcomes.

Materials and Methods

Patient demographics

From January 2000 to December 2010, patients who underwent colectomy after colonoscopic polypectomy for pT1 CRC were retrospectively enrolled from a prospectively maintained database. The database includes patient demographics (age, gender, ASA score, family history of CRC or polyposis disease, and pre-operative carcinoembryonic antigen (CEA) levels), surgical procedure, morbidity, mortality, duration of hospital stay, pathological features (number of harvested lymph nodes and lymph node metastasis) and follow-up status. The mean follow-up period was 64.0 ± 30.9 months.

Sixty-eight patients with pT1 colon cancer who had undergone polypectomy and then colectomy were included. The patients were divided into two groups according to extent of the resection: 27 in the limited colectomy group and 41 in the radical colectomy group.

Surgical techniques

Radical colectomy was defined as ligation of the vessels and dissection of the lymph node to the origin of the main vessels. For example, for sigmoid or descending colon cancer, the patient underwent anterior resection or left hemicolectomy with the inferior mesenteric vessels ligated above the left colic vessels. For tumors located at the cecum or ascending colon, the patient received right hemicolectomy with the vessels ligated near the superior mesenteric vessels. Then, for tumors located at the transverse colon, the patient received extended right hemicolectomy or transverse colon colectomy with ligation of the middle colic vessels near the superior mesenteric vessels. Otherwise, the operation was defined as limited colectomy. All patients underwent one-stage surgery without diverting colostomy or ileostomy. The decision of limited or radical resection was operator dependent.

Definition of tumor recurrence

Local recurrence was defined as recurrence at or near the anastomotic site. Distant metastasis was defined as recurrence at various distant organs or tissues. Recurrence was confirmed by histological examination of the tissue or progressive or new radiological findings, with or without elevation of tumor marker levels. The time to recurrence was defined as the interval between the time of surgical resection and the time of identification of the recurrence.

Statistical analysis

Continuous and categorical variables were compared between the groups using the ANOVA test and chi-square analysis when appropriate. Five-year survival rates were calculated using the Kaplan-Meier

method and compared using the log-rank test. Statistical significance was defined as $p < 0.05$. Statistical analyses were performed using the SPSS package (version 16.0 for Windows; SPSS, Chicago, IL, USA).

Results

Patient demographics, lymph node status, and treatment-related variables for both groups are shown in Table 1. No significant difference was found in age, gender, family history of CRC, ASA classification, pre-operative CEA levels, surgical methods, surgical complications, or duration of hospital stay between

Table 1. Patients' characteristics

Variables	Colon resection (%)		<i>p</i> value
	Limited (n = 27)	Radical (n = 41)	
Age (years)	64.4 ± 11.9	63.2 ± 12.1	0.977 ^b
Gender (M/F)			
Male	20 (74)	25 (61)	0.264 ^a
Female	7 (26)	16 (31)	
ASA classification			
I-II	22 (81)	36 (86)	0.471 ^a
III-IV	5 (19)	5 (14)	
Family history			
Yes	14 (52)	19 (46)	0.656 ^a
No	13 (48)	22 (54)	
Pre-operative CEA level			
≤ 5	25 (93)	38 (93)	0.989 ^a
> 5	2 (7)	3 (7)	
Surgical methods			
Open	16 (59)	27 (66)	0.581 ^a
Laparoscopy	11 (41)	14 (34)	
Surgical complication			
Absence	22 (81)	33 (80)	0.919 ^a
Presence	5 (19)	8 (20)	
Surgical mortality (patients)			
Yes	0 (0)	0 (0)	
Hospital stay (days)	9.5 ± 6.0	9.9 ± 14.3	0.603 ^b
LN harvest	7.3 ± 5.4	10.7 ± 6.9	0.034 ^b
Lymph nodes metastasis			
Yes	3 (11)	0 (0)	0.029 ^a
No	24 (89)	41 (100)	

LN: lymph nodes.

^a AS determined by chi square.

^b AS determined by ANOVA test.

the groups. However, more lymph nodes were harvested in the radical colectomy group (10.7 ± 6.9 vs. 7.3 ± 5.4 , $p = 0.034$), while more patients with lymph node metastasis were found in the limited colectomy group (11.1% vs. 0.0%, $p = 0.029$). The latter group also tended to have a higher recurrence rate (3.7% vs. 0.0%, $p = 0.214$) than the former (Table 2), although this difference was not significant. No surgery-related deaths occurred in either group.

Overall and disease-free survival

The 5-year overall survival rate and disease-free survival rate did not differ between the groups (95.5% in the limited colectomy group vs. 97.5% in the radical colectomy group, $p = 0.373$ and 0.354, respectively; Table 2, Figs. 1 and 2). Univariate analysis of

Table 2. Recurrence, lymph nodes metastasis and survival

Recurrence and survival	Colon resection (%)		<i>p</i> value ^a
	Limited (n = 27)	Radical (n = 41)	
Overall recurrence, n (%)	1 (3.7)	0	0.214 ^a
Time to recurrence (months)	85.7	NA	
5-year overall survival	95.50%	97.50%	0.373 ^b
5-year disease free survival	95.50%	97.50%	0.354 ^b

n: number of cases.

^a As determined by chi-squared tests.

^b As determined by Kaplan-Meier method.

NA: not available.

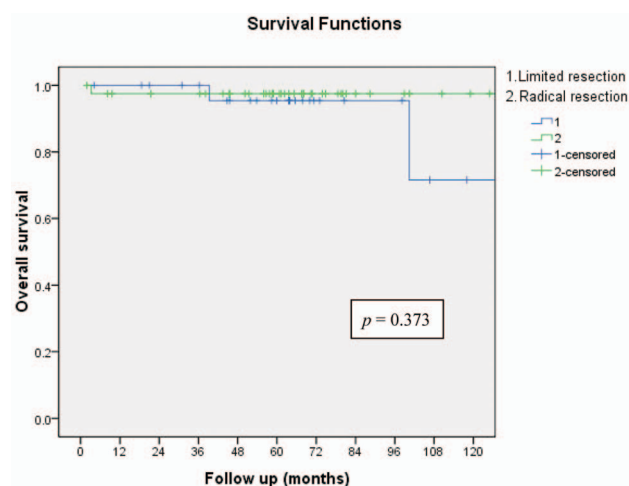


Fig. 1. Overall survivals of radical and limited resection for early colon cancer.

prognostic factors to examine overall survival showed that old age, high ASA scores, and the presence of surgical complications were poor prognostic factors, but multivariate analysis yielded no significant findings in this regard (Table 3). Univariate analysis of prognostic factors to determine disease-free survival showed that the presence of surgical complications indicated a poor prognosis, and this factor was found to

be significant in the multivariate analysis as well (Table 4). Of note, type of resection had marginal significance in the multivariate analysis, that is, limited colectomy tended to be associated with poor disease-free survival ($p = 0.0516$).

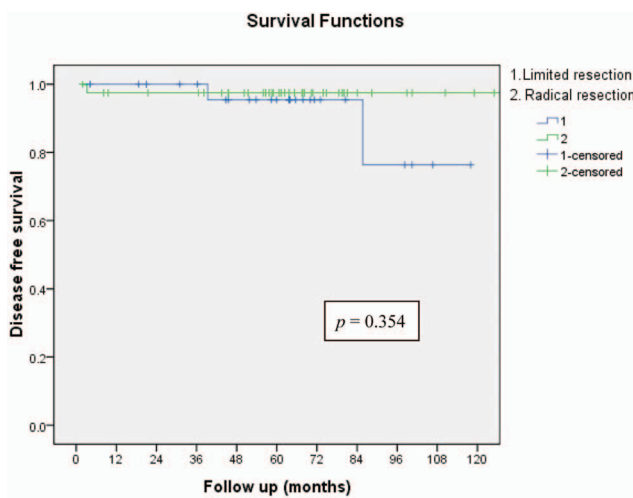


Fig. 2. Disease free survivals of radical and limited resection for early colon cancer.

Table 3. Prognostic factors influencing over-all survival rate after colectomy of malignant polyp

Univariate analysis	5-year survival rate (%)	p value ^a	Multivariate analysis p value ^a
Age (years)			
≤ 70	100	0.010	0.882
> 70	89.4		
Gender (M/F)			
Male	95	0.209	
Female	100		
Type of resection			
Radical	97.5	0.373	0.914
Limited	95.5		
ASA classification			
I-II	98.2	0.03	0.921
III-IV	45		
Surgical complication			
Yes	83.1	0.042	0.88
No	85.7		

^a AS determined by log-rank test.

Table 4. Prognostic factors influencing disease-free survival rate after colectomy of malignant polyp

Univariate analysis	5-year survival rate (%)	p value ^a	Multivariate analysis		
			p value ^b	HR	95%CI
Age (years)					
≤ 70	88.9	0.141	0.230	7.029	0.291- 169.997
> 70	89.4				
Gender (M/F)					
Male	95	0.236			
Female	100				
Type of resection					
Radical	97.5	0.354	0.0516	0.349	0.015- 8.356
Limited	95.5				
ASA classification					
I-II	87.3	0.534	0.655	0.516	0.028- 9.395
III-IV	90				
Surgical complication					
Yes	83.1	0.028	0.049	14.781	1.012- 215.856
No	90				

^a AS determined by log-rank test.

^b AS determined by Cox's proportional hazard model.

HR: Hazard ratio.

CI: Confidence interval.

Discussion

The choice of surgical treatment for early CRC is weighted by oncological outcome and surgical risk. In the present study, we examined the cases of patients diagnosed with T1 colon cancer after endoscopic resection and then underwent either radical or limited colectomy. Although the latter group had fewer lymph node harvested and more lymph node metastasis than the former group, the long-term survival did not differ between the groups. In addition, no significant difference was found in the surgical complication rate and mortality between the groups.

The NCCN recommends colectomy for pT1 cancer after colonoscopic polypectomy in the presence of unfavorable clinical and/or pathological findings such as sessile polyps, fragmented specimens, positive margins, grade 3-4, angio-lymphatic invasion, and deep submucosal invasion. Generally, patients have good prognosis with a recurrence rate of 1.3% after radical surgery.⁸ In the present study, the overall recurrence rate was 1.5%, which is consistent with that reported previously.⁸ Nonetheless, a trend towards increased recurrence was observed in the limited colectomy group (recurrence rate: radical colectomy vs. limited colectomy = 0% vs. 3.7%, $p = 0.214$), although lacking statistical significance.

A review of the literature revealed that lymph node metastasis occurred in approximately 3%-16.9% percent of patients with T1 colorectal carcinomas.¹⁰⁻¹² In our study, the percentage was 4.4% (3 in 68 patients), which was consistent with previously reported values. An interesting finding is that although the number of harvested lymph nodes was lower in the limited colectomy group (7.3 ± 5.4 vs. 10.7 ± 6.9 , $p = 0.034$), more patients in this group had lymph node metastasis (11.1% vs. 0%, $p = 0.029$). On further evaluation of the data, we found that in all cases, the lymph node metastasis developed in the paracolic nodes surrounding the tumor and therefore all the nodes had been removed en block with the tumor. This finding might also explain why we found no difference in long-term survival between the groups.

Several previous studies have reported a high ASA score and advanced age to be independent prog-

nostic factors for poor 5-year overall and disease-free survival after curative resection for colon cancer.¹³ In the present study, advanced age and high ASA scores were associated with a poor overall survival rate ($p = 0.01$ and 0.03 , respectively) in the univariate analysis, but not in the multivariate analysis. This discrepancy might have arisen because we included only early-stage CRC cases and the mean age of our patients were relatively lower than that of patients described in previous reports.¹⁴

In the univariate analysis, we found that surgical complications adversely affected both overall and disease-free survival rates ($p = 0.042$ and 0.028 , respectively), and this significance persisted with regard to the disease-free survival rate in the multivariate analysis. It is well known that surgical complications adversely affect not only short-term outcomes but also long-term survival after surgery for different kinds of cancers, including CRC.^{13,15,16} The mechanism generally proposed includes a period of immune suppression caused by a possible systemic inflammatory response to the complication. Some previous studies also showed that the presence of inflammatory cytokines and the subsequent downregulation of antigen-presenting cells could play an important role in metastasis.^{17,18} Torre et al. compared standard resection and segmental resection after endoscopic excision for pT1 lesions¹⁹ and found no differences in overall morbidity, mortality, or 5-year overall and disease-free survival between the groups. They concluded that segmental resection was a safe and effective alternative to standard resection. Similarly, in our study, the short-term outcomes (e.g., surgical complication and duration of hospital stay) did not differ between the radical and limited colectomy groups. Further, no surgery-related deaths were noted. Therefore, we agree with Torre et al.'s suggestion that limited colectomy could be an alternative to radical colectomy for pT1 colon cancer after endoscopic resection.

This study has some limitations. First, it was a retrospective study and a selection bias may exist. Second, the follow-up time was probably too short for assessment of long-term outcomes for early-stage CRC. Further studies with a larger sample size and longer

follow-up time (10 years or more) must be conducted in the future.

Conclusion

Although the number of harvested lymph nodes was lower with limited colectomy for pT1 colon cancer after endoscopic resection than with radical colectomy, no significant difference in short-term outcomes and long-term survival was found between the groups.

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原 著

經內視鏡切除術後的 pT1 大腸癌病人， 接受腸切除手術之長期預後探討

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目的 這項研究評估比較內視鏡切除術後的 pT1 大腸癌病患接受腸切除的長期存活。

方法 從 2000 年 1 月至 2010 年 12 月，經內視鏡切除術後的 pT1 大腸癌病患接受過腸切除手術治療的病患均收入研究。研究主要對於根除性腸切除及限制性腸切除兩組作分析，比較淋巴轉移，復發率及存活率。

結果 共計 68 位病患被納入這項研究。其中 27 位接受局限制性腸切除，另外 41 位接受根除性腸切除。局限制性腸切除組病人淋巴轉移比例較高 (11.1% vs. 0.0%, $p = 0.029$)。根除性腸切除組摘除的淋巴結數目較多 (10.7 ± 6.9 vs. 7.3 ± 5.4 , $p = 0.034$)，限制性腸切除組淋巴轉移率較高 (11.1% vs. 0.0%, $p = 0.029$)。兩組在復發率 (3.7% vs. 0.0%, $p = 0.214$)，五年整體存活率 (95.5% vs. 97.5%, $p = 0.373$) 及無病存活率 (95.5% vs. 97.5%, $P = 0.354$) 並沒有統計上的差異。

限制性腸切除組復發率有較高的趨勢 (3.7% vs. 0.0%, $p = 0.214$)。兩組均沒有因手術造成的死亡。手術併發症為較差預後的獨立影響因子，然而手術併發症在兩組間沒有差異。

結論 經內視鏡切除術後的 pT1 大腸癌病患，雖然限制性腸切除組淋巴轉移率較高，但是根除性腸切除組及限制性腸切除組在預後方面就復發率，整體存活率及無病存活率方面無差異。此外，兩組在手術併發症及死亡率方面無差異。

關鍵詞 pT1 大腸癌、根除性腸切除、限制性腸切除。