Original Article

Is More Intensive Abdominal Computed Tomography Scanning after Radical Resection for Stage II and III Colorectal Cancer Necessary?

Ming-Shan Su
Cheng-Wen Hsiao
Shu-Wen Jao
Chang-Chieh Wu
Chia-Cheng Lee
Tsai-Yu Lee
Division of Colon and Rectal Surgery, Department of Surgery, Tri-Service General Hospital, Taipei, Taiwan

Key Words
Colorectal cancer;
Resection;
Computed tomography

Purpose. Current National Comprehensive Cancer Network guidelines recommend abdominal computed tomography (CT) surveillance after radical resection for stage II or III colorectal cancer beginning 1 year after resection. However, this minimalist approach may not be sufficient. This study aimed to determine whether the incidence of disease recurrence or metastasis could justify more intensive abdominal CT after radical surgery.
Patients and Methods. We searched the Cancer Registry database of the Tri-Service General Hospital between January 2007 and December 2011 and analyzed the incidence of disease recurrence detected by using abdominal CT scanning. All patients undergoing radical resection for newly diagnosed colorectal cancer were included. Exclusion criteria were tumors of TNM stage 0, I or IV; lack of adequate staging to rule out distant or residual disease; and a lack of monitoring with a regular surveillance program.
Results. In total, 475 patients met the inclusion criteria; 237 and 238 patients had stage II and III disease, respectively. The overall tumor recurrence rate and the incidence of recurrences detected by using abdominal CT in the first year was 5.4% (n = 26) and 3.5% (n = 17), respectively.
Conclusion. After radical resection for stage II and III colorectal cancer, the incidence of abdominal CT-detected recurrences in the first year is rare (3.5%). Abdominal CT within the first year after radical resection for stage II and III colorectal cancer seems to be unnecessary. Furthermore, the incidence of recurrence is low in the first year (1.6% and 5.4%), and it remains low in the first 18 months, with incidences of 2.1% and 5.8% for stages II and III, respectively. In our study, it seems safe to extend the time until the first abdominal CT in stage II colorectal cancer after radical resection.
[*J Soc Colon Rectal Surgeon* (*Taiwan*) *2014;25:49-54*]

Colorectal cancer (CRC) is the second most common type of cancer in Taiwan and the third-leading cause of cancer mortality. Prognosis of these patients mainly depends on the tumor stage at diagnosis.

Received: March 12, 2014. Accepted: May 28, 2014.
Corresponding author: Dr. Cheng-Wen Hsiao, Division of Colon and Rectal Surgery, Department of Surgery, Tri-Service General Hospital, No. 325, Sec. 2, Chenggong Rd., Neihu District, Taipei 114, Taiwan. Tel: +886-2-8792-3311 ext. 88052; Fax: +886-2-8792-7292; Email: sod.su@yahoo.com.tw

In 75% of newly diagnosed cases, the tumor is confined to a portion of the bowel and regional lymph nodes. Complete removal of the tumor en-bloc with a portion of the normal bowel along with mesenteric and regional lymph nodes is considered a curative resection or radical surgery. However, up to 30-50% of patients with stage II-III tumors who undergo radical surgery will develop tumor relapse as a locoregional recurrence, distant metastasis, or as metachronous colorectal lesions after 5 years of follow-up.[1]

On the basis of the current National Comprehensive Cancer Network guidelines, computed tomography (CT) surveillance after radical resection for stage II or III CRC should begin 1 year after resection. However, for many discerning patients and physicians, particularly with respect to CRC, this minimalist approach has not been sufficient, and many doctors perform a more intensive examination. The aim of this study was to determine whether the incidence of recurrence or metastasis was high enough to justify more intensive abdominal CT scanning after radical resection.

Materials and Methods

We searched the Cancer Registry database of the Tri-Service General Hospital between January 2007 and December 2011. All patients undergoing radical resection for newly diagnosed CRC were included in this study. In total, 1,178 patients were identified from our database. Exclusion criteria were TNM stage 0, I or IV tumors; lack of an adequate staging to rule out distant or residual disease; not receiving radical resection; and an inability to be monitored by a regular surveillance program. We retrospectively analyzed the recurrences detected on abdominal CT scans at 3, 6, 9, 12, 15, and 18 months post-operation in 475 patients.

Results

During the study period, 475 patients met the inclusion criteria, with a mean age of 66 ± 14 years (range: 25-94 years). Of these, 256 (54%) patients were men, and 219 (46%) were women. There were 377 (79%) patients with colon cancer and 98 (21%) patients with rectal cancer. The final pathological staging included 237 (50%) stage II and 238 (50%) stage III cancers. The clinical features of patients are summarized in Table 1.

In 475 patients, there were 26 recurrences in 12 months and 33 recurrences in 18 months after radical surgery (Table 2). The tumor recurrence rate in first year was 5.4%, and it was 6.9% at 18 months after surgery.

The incidence of recurrences detected by using abdominal CT in the first year was 3.5% (n = 17); even at 18 months post-operation, the incidence was still low (4%, n = 19). Individually, there were 5 recurrences detected by using abdominal CT in cases of stage II CRC, including 3 in the liver and 2 in the regional lymph nodes (LN). In stage III CRC cases, 14 recurrences were detected by using abdominal CT. Twelve recurrences occurred in the liver, 1 in a re-

Table 1. Clinical features of patients

Parameter	Total (n = 475)
Age (years)	
Average ± SD	66 ± 14
Range	25-94
Sex, n (%)	
Male	256 (54%)
Female	219 (46%)
Tumor location, n (%)	
Colon	377 (79%)
Rectum	98 (21%)
Tumor TNM stage	
Stage II	237 (50%)
Stage III	238 (50%)
Chemotherapy#	
Stage II	178 (75%)
Stage III	195 (82%)
Degree of differentiation	
Well	48 (10%)
Moderate	366 (77%)
Poor	61 (13%)
Increased serum CEA level*	118 (24%)

Including oral and intravenous chemotherapy.

* CEA: carcinoembryonic antigen; The upper limit of normal range of carcinoembryonic antigen (CEA) concentration was 5 ng/mL.

SD = standard deviation.

Table 2. Sites of recurrent disease for colorectal cancer within 18 months after surgery

Site of recurrence	Numbers of patients with recurrence by the months after surgery						
Months	3	6	9	12	15	18	Total
Intra-abdominal metastasis							
Detected by using abdominal CT							
Liver	2	4	2	4	1	1	14
Omentum			1				1
Distal lymph nodes		1					1
Regional lymph nodes		1	1	1			3
Detected by using colonoscopy							
Anastomosis		1		3			4
Extra-abdominal metastasis							
Lung		1		2	3	1	7
Brain	1				1		2
Bone			1				1
Total	3	8	5	10	5	2	33

gional LN, 1 in a distal LN, and 1 in the omentum. The recurrence curves grouped according to the cancer stage are shown in Fig. 1.

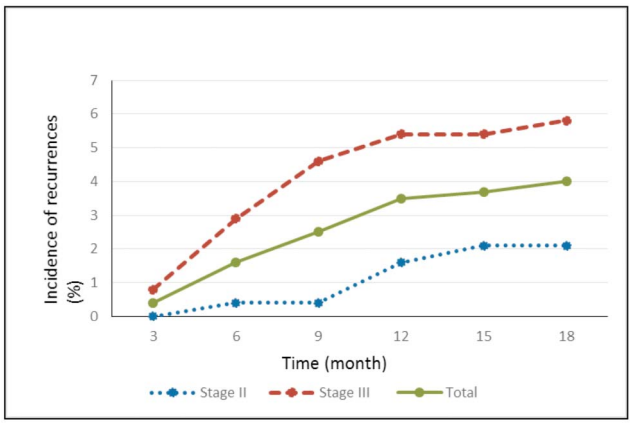

Fig. 1. The incidence of recurrences detected by using abdominal computed tomography grouped according to cancer stage.

Discussion

In spite of undergoing radical surgery, approximately half of the patients with CRC may develop recurrent disease, and their median survival does not exceed 2 years.[2-5] Most of these recurrences occur in patients who, at initial staging, had a tumor invading across the bowel wall causing perforation of the bowel, adhesion, invasion of neighboring organs (stage IIb and IIc disease), or had LN metastases (stage III disease). Besides disease recurrence, patients with CRC are considered to be at a higher risk for developing a second or metachronous bowel cancer,[6-11] particularly if they are aged ≤ 60 years.[9,10]

The time from initial treatment to recurrence and the initial stage are important prognostic factors in patients with recurrent colon cancer.[12] Follow-up programs for patients with curatively resected CRC help to improve survival. These follow-up programs include regular visits and performance of blood carcinoembryonic antigen (CEA) testing, chest radiography, colonoscopy, and liver imaging; however, it is not clear which tests or frequency of visits are optimal. It has been suggested that improved survival is owing to the diagnosis of recurrence at an earlier, asymptomatic stage, which allows for more curative resection of the recurrence. Patients should be made aware of the risk of disease recurrence or secondary bowel cancer, the potential benefits of follow-up, and the uncertainties requiring further clinical trials.

Advantages of a more intensive follow-up of patients with stage II and stage III disease have been shown prospectively in several older studies[13-15] and in 3 meta-analyses of randomized controlled trials designed to compare low- and high-intensity programs of surveillance.[16-19] Intensive postoperative surveillance has also been suggested to be of benefit to patients with stage I and IIA disease.[20] Furthermore, a population-based report indicated increased rates of resectability and survival in patients treated for local recurrence and distant metastases of CRC in more recent years, thereby providing support for more intensive post-operative follow-up in these patients.[21] However, preliminary results from a recent, randomized controlled trial show no overall mortality benefit of an intensive surveillance program for patients with resected stage I-III disease.[22] The authors found no benefit of regular monitoring with both CEA tests and on CT scans and concluded that CEA testing every 3-6 months combined with a single CT scan of the chest,

abdomen, and pelvis at 12-18 months is likely a cost-effective surveillance schedule. Clearly, controversies remain regarding the selection of optimal strategies for following patients after potentially curative CRC surgery, and the panel's recommendations are based mainly on consensus.[23,24] There are few studies focusing on the detection rate and timing of the initiation of CT surveillance.

In the current study, we demonstrated that the incidence of recurrences detected by abdominal CT in patients with stage II and III CRC who undergo a radical surgery was as low as 3.5% (n = 17) in first year post-surgery. If the data were grouped by cancer stage, in the stage II patients, the incidence was lower with 1.6% (n = 4) in first year; even at 18 months post-operation, the rate was still low at 2.1% (n = 5). In stage III patients, the incidence was 5.4% (n = 13) in the first year post-operation and 5.8% (n = 14) at 18 months post-operation. The proportion of patients diagnosed with recurrence was higher in stage III than in stage II disease, and the difference persisted in 18 months follow-up. Furthermore, in the reports of abdominal CT scanning performed 6 months post-operation, the high incidence of inflammatory changes, including fatty stranding, increasing numbers or enlargement of LN, and bowel wall thickening, was also noted in 32% of cases. The incidence is higher in rectal cancer at 45%. The false-positive results owing to inflammatory changes caused by surgery and chemoradiotherapy will lead to unnecessary radiation exposure with repeated CT scanning, as well added stress and other risks of unnecessary treatments.

Conclusions

Although many patients view follow-up as important, even if recurrence is not detected earlier, testing that is poorly justified can lead to both psychological and physical harm to patients as well as unnecessary costs. In our study, the incidence of abdominal CT-detected recurrences in the first year was rare (3.5%), and a more intensive examination schedule tended to be unnecessary. Furthermore, in stage II and stage III CRC, the incidence was low in the first year (1.6% and 5.4%), and it remained low at 18 months at 2.1% and 5.8% in stage II and III disease, respectively. On the basis of our study, it appears to be safe to extend the time to the first abdominal CT in stage II CRC after radical resection.

References

1. Safi F, Beyer HG. The value of follow-up after curative surgery of colorectal carcinoma. *Cancer Detect Prev* 1993;17: 417-24.
2. Griffin MR, Bergtralh EJ, Coffey RJ, Beart RW, Melton LJ 3rd. Predictors of survival after curative resection of carcinoma of the colon and rectum. *Cancer* 1987;60:2318-24. doi: 10.1002/1097-0142(19871101)60:9<2318::AID-CNCR2820600934>3.0.CO;2-B
3. Berge T, Ekelund G, Mellner C, Pihl B, Wenckert A. Carcinoma of the colon and rectum in a defined population. *Acta Chir Scand* 1973;438:Suppl:1-86.
4. Weinerman BH, Orr KB. Colorectal cancer: total provincial experience with survival analysis. *Can J Gastroenterol* 1989; 3:126-30.
5. Galandiuk S, Wieand HS, Moertel CG, Cha SS, Fitzgibbons RJ Jr, Pemberton JH, et al. Patterns of recurrence after curative resection of carcinoma of the colon and rectum. *Surg Gynecol Obstet* 1992;174:27-32.
6. Enblad P, Adami HO, Glimelius B, Krusemo U, Pahlman L. The risk of subsequent primary malignant diseases after cancers of the colon and rectum. A nationwide cohort study. *Cancer* 1990;65:2091-100. doi: 10.1002/1097-0142(19900501)65:9<2091::AID-CNCR2820650934>3.0.CO;2-M
7. Bulow S, Svendsen LB, Mellemgaard A. Metachronous colorectal carcinoma. *Br J Surg* 1990;77:502-5. doi: 10.1002/bjs.1800770509
8. Cali RL, Pitsch RM, Thorson AG, Watson P, Tapia P, Blatchford GJ, et al. Cumulative incidence of metachronous colorectal cancer. *Dis Colon Rectum* 1993;36:388-93. doi: 10.1007/BF02053945
9. Evans HS, Moller H, Robinson D, Lewis CM, Bell CMJ, Hodgson SV. The risk of subsequent primary cancers after colorectal cancer in southeast England. *Gut* 2002;50:647-52. doi: 10.1136/gut.50.5.647
10. Shureiqi I, Cooksley CD, Morris J, Soliman AS, Levin B, Lippman SM. Effect of age on risk of second primary colorectal cancer. *J Natl Cancer Inst* 2001;93:1264-6. doi: 10.1093/jnci/93.16.1264
11. Green RJ, Metlay JP, Propert K, Catalano PJ, Macdonald JS, Mayer RJ, Haller DG. Surveillance for second primary colorectal cancer after adjuvant chemotherapy: an analysis of Intergroup. *Ann Int Med* 2002;136:261-9. doi: 10.7326/0003-4819-136-4-200202190-00005

12. O'Connell MJ, Campbell ME, Goldberg RM, Grothey A, Seitz JF, Benedetti JK, Andre T, Haller DG, Sargent DJ. Survival following recurrence in stage II and III colon cancer: findings from the ACCENT data set. *J Clin Oncol* 2008;26: 2336-41. doi: 10.1200/JCO.2007.15.8261
13. Pietra N, Sarli L, Costi R, Ouchemi C, Grattarola M, Peracchia A. Role of follow-up in management of local recurrences of colorectal cancer: a prospective, randomized study. *Dis Colon Rectum* 1998;41:1127-33. doi: 10.1007/BF02239434
14. Rodriguez-Moranta F, Salo J, Arcusa A, Boadas J, Piñol V, Bessa X, et al. Postoperative surveillance in patients with colorectal cancer who have undergone curative resection: a prospective, multicenter, randomized, controlled trial. *J Clin Oncol* 2006;24:386-93. doi: 10.1200/JCO.2005.02.0826
15. Secco GB, Fardelli R, Gianquinto D, Bonfante P, Baldi E, Ravera G, et al. Efficacy and cost of risk-adapted follow-up in patients after colorectal cancer surgery: a prospective, randomized and controlled trial. *Eur J Surg Oncol* 2002;28: 418-23. doi: 10.1053/ejso.2001.1250
16. Desch CE, Benson AB 3rd, Somerfield MR, Flynn PJ, Krause C, Loprinzi CL, et al. American Society of Clinical Oncology. Colorectal cancer surveillance: 2005 update of an American Society of Clinical Oncology practice guideline. *J Clin Oncol* 2005;23:8512-9. doi: 10.1200/JCO.2005.04.0063
17. Figueredo A, Rumble RB, Maroun J, Earle CC, Cummings B, McLeod R, et al. Follow-up of patients with curatively resected colorectal cancer: a practice guideline. *BMC Cancer* 2003;3:26-39.
18. Jeffery M, Hickey BE, Hider PN. Follow-up strategies for patients treated for non-metastatic colorectal cancer. *Cochrane Database Syst Rev* 2007:CD002200. doi: 10.1002/14651858.CD002200.pub2
19. Renehan AG, Egger M, Saunders MP, O'Dwyer ST. Impact on survival of intensive follow up after curative resection for colorectal cancer: systematic review and meta-analysis of randomised trials. *BMJ* 2002;324:813-20. doi: 10.1136/bmj.324.7341.813
20. Tsikitis VL, Malireddy K, Green EA, Christensen B, Whelan R, Hyder J, et al. Postoperative surveillance recommendations for early stage colon cancer based on results from the clinical outcomes of surgical therapy trial. *J Clin Oncol* 2009;27:3671-6. doi: 10.1200/JCO.2008.20.7050
21. Guyot F, Faivre J, Manfredi S, Meny B, Bonithon-Kopp C, Bouvier AM. Time trends in the treatment and survival of recurrences from colorectal cancer. *Ann Oncol* 2005;16:756-61. doi: 10.1093/annonc/mdi151
22. Primrose JN, Perera R, Gray A, Rose P, Fuller A, Corkhill A, et al. Effect of 3 to 5 years of scheduled CEA and CT follow-up to detect recurrence of colorectal cancer: the FACS randomized clinical trial. *JAMA* 2014;311:263-70. doi: 10.1001/jama.2013.285718
23. Pfister DG, Benson AB 3rd, Somerfield MR. Clinical practice. Surveillance strategies after curative treatment of colorectal cancer. *N Engl J Med* 2004;350:2375-82. doi: 10.1056/NEJMcp010529
24. Li Destri G, Di Cataldo A, Puleo S. Colorectal cancer follow-up: useful or useless? *Surg Oncol* 2006;15:1-12. doi: 10.1016/j.suronc.2006.06.001

原　著

第二及第三期大腸直腸癌根除手術後是否需要更密集的追蹤腹部電腦斷層？

蘇明山　蕭正文　饒樹文　吳昌杰　李家政　李才宇

三軍總醫院　外科部　大腸直腸外科

背景　根據目前的 NCCN 指引，在第二期和第三期的大腸直腸癌接受完根除手術，腹部電腦斷層追蹤建議從一年後開始，但是很多病人和醫師並不會滿足這樣的最基本的追蹤。本篇研究的目的在於評估腫瘤復發率是否夠高而需要執行更密集的術後腹部電腦斷層檢查。

方法　從三軍總醫院的癌症登記資料庫搜尋，從 2007 年 1 月到 2011 年 12 月，在單一醫學中心診斷的出的第二和第三期大腸直腸癌，至少接受根除手術治療，從術後開始至第十八個月止，發生可被腹部電腦斷層偵測出的腫瘤復發或轉移的發生率。

結果　總計 475 位病人符合篩選條件，其中 256 人為男性，219 人為女性，平均年齡為 66 歲。有 237 位為大腸直腸癌第二期，238 人為第三期。第一年的腫瘤復發率為 5.4%，如果僅計算可被腹部電腦斷層偵測到的轉移，第一年則為 3.5%。

結論　第二期及第三期大腸直腸癌的追蹤，在一年內發生可被腹部電腦斷層偵測到轉移的機率是很低的 (分別是 1.6% 及 5.4%)，在第十八個月也僅 2.1% 及 5.8% 所以採用更密集的追蹤腹部電腦斷層顯示並不需要，而且術後第一次接受電腦斷層的時間再延長似乎也是安全的。

關鍵詞　大腸直腸癌、術後追蹤、電腦斷層掃描。