Surgery for Pulmonary Metastases from Colorectal Cancer

The Importance of Prethoracotomy Serum Carcinoembryonic Antigen as an Indicator of Prognosis

Objective: **Several investigators have analyzed prognostic factors of surgical treatment for pulmonary metastases from colorectal cancer, but the results remain inconclusive. This study was performed to determine the prognostic implications of the prethoracotomy serum level of carcinoembryonic antigen (CEA) in relation to the postthoracotomy recurrent pattern among patients with this disease.** ***Methods:*** **A retrospective analysis of prognostic factors was undertaken in 100 patients who had consecutively undergone initial surgical resection for pulmonary metastases of colorectal origin.** ***Results:*** **The overall 3- and 5-year survival rates were 62.2% and 49.4%, respectively. Univariate analysis revealed that the prethoracotomy serum CEA level and operative curability were strongly associated with prognosis, while in multivariate analysis, only the prethoracotomy serum CEA level was a significant prognostic indicator. Patients with a high level of prethoracotomy serum CEA more frequently exhibited recurrence in extrathoracic sites, especially in the brain.** ***Conclusion:*** **Before thoracotomy for pulmonary metastases from colorectal cancer, the serum CEA level was the most useful prognostic factor. Patients with elevated serum CEA level should undergo a careful prethoracotomy systemic survey and postthoracotomy follow-up for extrathoracic metastases, in particular brain metastases, and an appropriate combined therapeutic modality should be considered. (Jpn J Thorac Cardiovasc Surg 2003; 51: 289–296)**

Key words: serum carcinoembryonic antigen, pulmonary metastasis, pulmonary metastasectomy, colorectal cancer, prognosis

Masahiko Higashiyama, MD, Ken Kodama, MD, Naozumi Higaki, MD, Koji Takami, MD, Kohei Murata, MD,* Masao Kameyama MD,* and Hideoki Yokouchi, MD**.

Surgical resection is frequently performed for pulmonary metastases from various malignant tumors.[1-5] In fact, for some cancers, pulmonary metastasectomy is considered to prolong survival, and potentially cure this disease.[1-5] In our institute, pulmonary metastasectomy from various types of malignancy has been aggressively performed with favorable results by improving surgical techniques.[6-8] Thus, the role of pulmonary metastasectomy will continue to evolve with improvements in systemic treatment, although the criteria for patient selection remain undetermined.

Surgical resection for pulmonary metastases from colorectal cancer is the most commonly performed operation with a relatively favorable prognosis.[9-24] Several investigators[10,11,14,20,21,24] have analyzed prognostic factors of surgical treatment for this disease, and some promising clinicopathological variables influencing prognosis were proposed. However, because of the differences in the diagnostic modality of computed tomography, surgical techniques, and perioperative follow-

From the Department of Thoracic Surgery, *Department of Surgery, Osaka Medical Center for Cancer and Cardiovascular Diseases, and the **Department of Surgery, Suita Municipal Hospital, Osaka, Japan.

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Address for reprints: Masahiko Higashiyama, MD, Department of Thoracic Surgery, Osaka Medical Center for Cancer and Cardiovascular Diseases, 1-3-3, Nakamichi, Higashinari-ku, Osaka 537-8511, Japan.

up for this disease, a consensus for prognostic analysis has not been reached. In fact, multivariate prognostic analysis using prognosis-associated variables was not performed in most reports. In addition, there have been few investigations regarding the postthoracotomy-recurrent pattern in relation to prognosis.[10,15-17,23]

Recently, the prethoractomy serum level of carcinoembryonic antigen (CEA) has been suggested to be a potential prognostic indicator in patients undergoing metastasectomy with this disease.[13,20-24] However, why patients with a high level of prethoracotomy serum CEA may show a poor prognosis has not yet been clarified. This study was retrospectively performed to clarify the prognostic implications of this marker, prethoractomy serum CEA, by reviewing the postthoracotomy-recurrent pattern in this disease, and other prognosis-associated variables.

Subjects and Methods

Patient characteristics. Between January 1981 and September 2001, a total of 100 patients consecutively underwent initial resection for pulmonary metastases from colorectal cancer at our institute. The patient characteristics are summarized in Table I. No data were available in 7 patients as to the primary tumor stage, and 3 as to histological grade, because the primary surgery had been performed elsewhere.

Preparation for thoracotomy consisted of a chest CT scan to estimate pulmonary lesions, abdominal CT scan or ultrasonography, if necessary a brain CT scan, and bone scintigraphy during the follow-up period between detection of pulmonary lesions and the initial thoracotomy. Chest CT scans were performed at least twice or more before thoracotomy at intervals of at least more than two months to check for abnormal intrathoracic findings, especially pulmonary lesion number and mediastino-hilar node swelling.

Based on the above examination data, criteria for pulmonary metastasectomy were: 1) unilateral or bilateral pulmonary lesions seen on chest radiography or CT scan without bulky mediastino-hilar lymph node involvement, and indicated for resection, that is, potentially complete resection; 2) no extrathoracic distant metastasis and potentially satisfactory local control for primary colorectal lesions; and 3) possibly complete resection of both hepatic and pulmonary metastases, if present.

7 patients showed mediastino-hilar node swelling on preoperative chest CT scans, and 29 had a past history of surgical treatment and/or current extrathoracic recurrent lesions; 7 patients with primary local failure, 17 with metastases in the liver, 1 in the adrenal gland, 1 in the thyroid grand, 1 in the brain, 1 in the diaphragm and 1 in the chest wall. 3 patients synchronously underwent surgical treatment for the primary lesion and pulmonary metastases, and 5 simultaneously underwent surgery for pulmonary metastases and extrathoracic recurrence.

The median prethoracotomy serum CEA of the patients was 3.3 ng/ml, and the mean was 12.3 ng/ml, ranging from 1 to 288 ng/ml. According to this level, the patients were classified into three groups: 55 patients showed normal preoperative serum CEA levels (less than 5 ng/ml), and 23 showed borderline levels (between 5 and 10ng/ml), while 22 showed high levels (10 and higher than 10ng/ml).

The surgical mode at the initial thoracotomy is described in Table I. Node dissection or sampling was performed during lobectomy and pneoumonectomy, but was not performed in wedge resection, except when node swelling was observed on a chest CT scan.

Based on the surgical data file, the metastatic lesion numbers were as follows: a solitary lesion in 55 patients, and multiple lesions in 45 patients. Node involvement was observed in 12 patients, 6 of whom showed metastases at the mediastinal level (N2). Potentially curative surgery was performed in 94 patients, whereas 6 patients showed non-curative surgery due to the following reasons: pleural dissemination in 4, residue of pulmonary micrometastases in 1, and residue of mediastinal node involvement in 1.

Perioperative chemotherapy at thoracotomy, including preoperative and/or postoperative adjuvant therapy, was performed in 53 patients. 5-fluorouracil and its derivatives were administered in 47 patients: Tegaful in 23 patients, Doxifluridine in 16, Fluorouracil in 4, Carmofur in 2, and UFT in 2. Cisplatin-based chemotherapy was given to 4 patients, 3 of whom underwent postoperative intrathoracic chemothermotherapy because of pleural dissemination. Irinotecan-based chemotherapy was performed in 2 patients.

Repeated thoracotomy for pulmonary metastasectomy after the initial thoracotomy was performed in 13 patients; twice repeated thoracotomy in 11, and thoractomy three times in two.

Patient follow-up and analytic methods. Follow-up was available for all patients. Information was obtained from the patients' records by correspondence with the patients and their physicians, and from death certificates. Follow-up periods of the surviving patients ranged from 3.6 months to 168.7 months, and the median value was 30.3 months. We were able to ascertain the cause of death in all but 3 patients.

Table I. *Patient characteristics*

Gender	Male/Female	61/39
Age at initial thoracotomy (years)		39–79 (mean 60.3)
Primary tumor	Dukes' B/C/D/Unknown	33/52/8/7
	Location Colon/Rectum	44/56
	Histology Well/Moderate/Mucinous/Unknown	47/48/2/3
History or coexisting of extrathoracic recurrent lesions		
	No/Primary local/Liver/Others	71/7/17/ 5
Interval between primary resection and thoracotomy (years)		0–11.7 (mean 2.9)
Lesion number on preoperative radiography		1–8
	One/Two/Three/Four/Five/Six and more	49/25/18/4/1/3
Clinical mediastino-hilar node swelling on preoperative radiography		
	No/Yes	93/7
Site of lesions	Unilateral/Bilateral	79/21
Maximum tumor size (cm)		0.2–11.0
	Three and smaller/Larger than 3	59/41
Prethoracotomy serum CEA level (ng/ml)		1–288
	Normal (less than 5)/Borderline (5–10)/High (10 and more)	55/23/22
Lesion number at surgery		1–12
	One/Two/Three/Four/Five/Six or more	55/23/14/3/2/3
Surgical mode		
	Wedge/Lobectomy/Combined/Pneumonectomy	61/27/9/3
Mediastino-hilar node involvement	No/Yes	88/12
Pleural involvement	No/Yes	81/19
Curability	Yes/No	94/6
Perioperative chemotherapy	No/Yes	47/53
Repeated thoracotomy after initial thoracotomy	No/Yes	87/13

The site of the first recurrence after thoracotomy was also examined in the current series. Especially, in order to check on recurrent pulmonary metastases, post-thoracotomy follow-up was aggressively performed on chest X-ray and/or chest CT scans. When physical symptoms did not develop, clinical examination to detect extrathoracic distant metastases, such as bone and brain metastases, was not routinely performed, but was done as required. In contrast, ultrasonography to check the upper abdomen was performed every 6 to 12 months.

Kaplan-Meier estimated overall survival curves were calculated using the log-rank test, and multivariate Cox's proportional hazards regression analysis was performed using the StatView Ver. 5 computed system. The Chi-square test was used to determine statistical significance. Statistical significance was taken at p values less than 0.05.

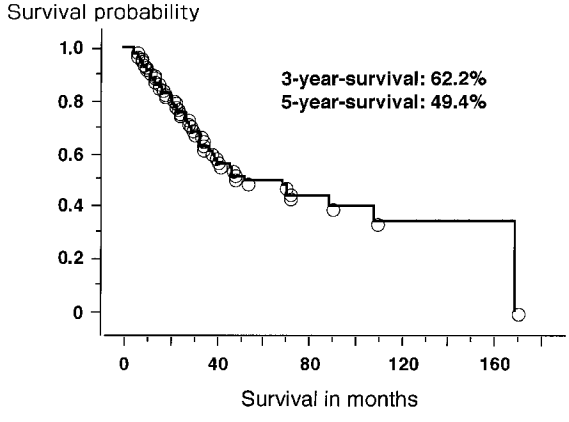

Fig. 1. Overall survival curve after the initial thoracotomy for pulmonary metastasectomy of colorectal cancer.
Three-year and 5-year-survival rates were 62.2% and 49.4%, respectively.

Results

Overall survival of patients. The overall survival curve is shown in Fig. 1. The 3-year and 5-year-survival rates were 62.2% and 49.4%, respectively.

Univariate analyses of prognosis. A summary of univariate prognostic analyses using prethoracotomy and thoracotomy-associated variables is shown in Tables II and III, respectively. Prognostic significance

Table II. *Univariate analysis of prognosis – Prethoracotomy variables –*

Variables		*No. of patients*	*5-year survival (%)*	*p value*
Gender	Male/Female	61/39	42.5/60.2	0.131
Age at thoracotomy	Younger than 61/61 and elder			
		49/51	57.5/40.4	0.079
Primary tumor				
Dukes' stage	B/C, D/Unknown	33/60/7	48.2/51.8*	0.720
Location	Colon/Rectum	44/56	44.5/53.3	0.975
Histology	Well/Moderate and mucinous/Unknown			
		47/50/3	45.4/52.8*	0.642
History of surgical treatment and/or current coexistence for extrathoracic metastasis				
	No/Yes	71/29	54.7/35.1	0.075
Interval between primary resection and thoracotomy (years)				
	Shorter than three/Three and longer			
		59/41	59.3/36.7	0.130
Lesion number on preoperative X-ray tomography or CT scan				
	Solitary/Multiple	49/51	53.3/46.7	0.735
Increase of lesion number on X-ray tomography or CT scan through follow-up periods before thoracotomy				
	No/Yes	77/23	53.2/39.3	0.128
Site	Unilateral/Bilateral	79/21	50.1/48.8	0.960
Maximum tumor size (cm)				
	Three and smaller/Larger than three			
		63/37	50.3/46.8	0.398
Serum CEA level (ng/ml)				
	Less than 5 / 5 and higher	55/45	60.4/34.1	0.024
	Less than 10 / 10 and higher	78/22	54.6/29.7	0.018

*Data excluding unknown cases

Table III. *Univariate analysis of prognosis – Thoracotomy-associated variables –*

Variables		*No. of patients*	*5-year survival (%)*	*p value*
Number of metastatic lesions at surgery				
	Solitary/Multiple	55/45	51.7/47.5	0.846
	One or two/Three or more	78/22	55.1/29.1	0.242
Mediastino-hilar node involvement				
	No/Yes	88/12	51.4/33.5	0.106
Pleural involvement	No/Yes	81/19	51.5/39.6	0.211
Resection	Wedge/Others	61/39	47.3/51.3	0.688
Curability	Yes/No	94/6	52.3/0	0.041
Perioperative chemotherapy				
	No/Yes	47/53	41.9/53.5	0.411

was observed in serum CEA level (less than 5ng/ml vs. 5ng/ml and higher, $p = 0.024$, less than 10ng/ml vs. 10ng/ml and higher, $p = 0.018$) among prethoracotomy variables, and operative curability (curative vs. non-curative, $p = 0.041$) among thoracotomy-associated variables.

Prognosis among the three groups: normal, borderline, and high level of prethoracotomy serum CEA. As described above, since patients with high levels of serum CEA level showed significantly poor prognosis, overall survival curves according to the serum CEA level in the three groups were examined. In Fig. 2, there was also a significant correlation of prognosis among the three groups (normal, borderline, and high level: log-rank test, $p = 0.031$).

Multivariate analysis of prognosis. Cox's proportional hazards regression analysis of prognosis using the above two variables, prethoracotomy serum CEA

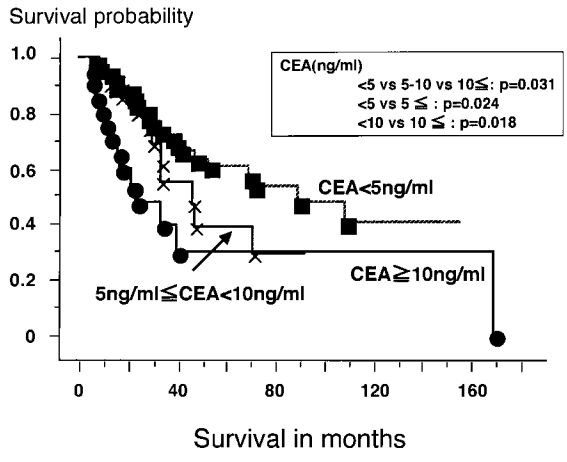

Fig. 2. Overall survival curves of pulmonary metastasectomy of colorectal cancer according to the prethoracotomy serum CEA level.
Overall survival curves according to three groups of prethoracotomy serum CEA level are shown. There was a statistically significant correlation of prognosis among the three groups: normal, borderline, and high level (log-rank test, p = 0.031).

Table IV. *Multivariate analysis of prognosis –Cox's proportional hazards regression analysis–*

Variables	*Hazard ratio*	*95%CI*	*p value*
Model 1			
Curability (Yes versus No)			
	0.395	0.138–1.133	0.084
Serum CEA level (less than 5 ng/ml versus 5 and higher ng/ml)			
	0.525	0.287–0.961	0.037
Model 2			
Curability (Yes versus No)			
	0.431	0.148–1.250	0.121
Serum CEA level (less than 10 ng/ml versus 10 and higher ng/ml)			
	0.490	0.247–0.972	0.041

CI, Confidence interval.

level and operative curability, by two models (Model 1: normal CEA level vs. borderline and high CEA level, Model 2: normal and borderline CEA level vs. high CEA level), showed that only the former variable was a significantly independent prognostic factor (Model 1: Hazard ratio: 0.525, 95% Confidence interval: 0.287–0.961, p = 0.037, Model 2: Hazard ratio: 0.490, 95% Confidence interval: 0.247–0.972, p = 0.041, Table IV).

Prethoracotomy serum CEA level and recurrent pattern after thoracotomy. Table V shows a recurrent pattern after thoracotomy according to the serum CEA level. The patients with high levels of serum CEA (10ng/ml and high) exhibited extrathoracic distant recurrence significantly more frequently than those with normal and borderline levels (p = 0.003, Chi-square test).

The initial site in extrathoracic distant recurrence was the brain in 13 patients, the bone in 8, the liver in 9, and other sites in 3 (adrenal gland in 2 and ovary in 1). Regarding these recurrences, the incidence of brain metastasis was significantly higher in the patients (27%) with high levels of serum CEA than that in those (9%) with normal and borderline levels (p = 0.024, Chi-square test, Table V).

Discussion

According to recent reports describing pulmonary metastasectomy for patients with colorectal cancer, the 5-year overall survival rate after thoracotomy ranges about from 20% to 50%.[10-14,18-20,22,23] In the present study, it was 49.4%, showing relatively more favorable surgical results, especially for a Japanese series. Nev-

Table V. *Recurrence after thoracotomy*

	Serum CEA level before thoracotomy	
	CEA<10ng/ml N=78 (%)	*CEA≧10ng/ml N=22 (%)*
Recurrent pattern		
None	32	6
Intrathoracic alone		
PM	15 (19)	1 (5)
PM and intrathoracic local	5 (6)	0
Intrathoracic local	3 (4)	1 (5)
Intrathoracic and extrathoracic		
PM and distant	12 (15)	6 (27)
PM and abdominal local	1 (1)	1 (5)
Intrathoracic local and distant	2 (3)	0
Extrathoracic alone		
Distant	6 (8)	7 (32)
Abdominal local	2 (3)	0
*Rate of extrathoracic distant metastases**	20 (25)	13 (59)
Site in extrathoracic distant recurrence		
Brain**	7 (9)	6 (27)
Bone	5	3
Liver	7	2
Others	1	2

PM, Recurrent pulmonary metastases.
* p = 0.003 (Chi-square test) ** p = 0.024 (Chi-square test)

ertheless, this survival rate may depend on the surgical indication criteria: For example, if pulmonary metastasectomy is performed for patients with more advanced conditions such as bulky nodal involvement, miliary metastatic nodules, and malignant pleural effusion, surgical results may be unfavorable. Therefore, when discussing the surgical results of this disease, the patients' backgrounds and surgical indication of pulmonary metastasectomy for this disease must be considered. The present study in one institute was performed under a rigid surgical criteria and follow-up. For example, it is important that patients with bulky mediastino-hilar lymph node involvement on preoperative thin-section CT scans, namely those with potential "clinical-N2" disease, are principally excluded from pulmonary metastasectomy. In this respect, surgical results based on a multicenter retrospective analysis may be not so reliable, despite a relatively large number of patients.[4]

Prognostic analyses of pulmonary metastasectomy for this disease have been performed by many investigators,[10,11,14,20,21,24] and various clinicopathological variables were proposed as candidate prognostic indicators, such as metastatic lesion number,[9-12,15-21,24] maximum tumor size,[11,17] intrathoracic node involvement,19 metastases in an extrathoracic site,[19] interval between primary surgery and thoracotomy,[18,24] surgical curability[14,20] and prethoracotomy serum CEA level.[13,20,22-24] However, the prognostic significance of the metastatic lesion number remains to be clarified. For example, patients with solitary metastasis[9-12,16,17,19-21,24] or those with 3 or fewer lesions[15,18] showed good prognosis. In the present series, metastatic lesion number, especially solitary or multiple at the initial pulmonary metastasectomy, did not influence postoperative survival. Therefore, the baseline metastatic lesion number for surgical indication has not yet been established, but 2 or less may be a reasonable lesion number. In our experience, when the metastatic number was 3 or more, some unfavorable factors, oncologically and surgically, were often combined in such patients.

In the present study, using not only univariate, but also multivariate analyses, the prethoracotomy CEA level in this disease was the most important prognostic factor, supporting the results previously reported by several investigators.[13,20-24] Experimentally, CEA may functionally participate in intercellular recognition and attachment with regard to potential promotion of metastatic spread of malignant cells, suggesting that CEA itself is strongly associated with the grade of tumor malignancy.[25] Clinically, it has been well noted

that patients with various kinds of malignant tumors have poor prognosis, in surgical as well as non-surgical conditions, when the serum CEA level was elevated. Thus, it may be important to examine the postthoracotomy recurrent pattern of this disease.

The patients with high prethoracotomy serum CEA levels showed more frequent postthoracotomy extrathoracic recurrence, especially in the brain. The metastases in this site are usually serious in terms of quality of life (QOL), and easily result in critical conditions. Therefore, the prognostic significance of the prethoracotomy serum CEA level might be closely associated with such unfavorable recurrent events. Thus, a high prethoracotomy serum CEA level in patients is potentially associated with a more systemic or extrathoracic spread of colorectal cancer disease. Considering these results, a careful prethoracotomy systemic survey and postthoracotomy follow-up for extrathoracic, metastases, especially brain metastases, may be required in patients with high serum CEA level, and an appropriate combined therapeutic modality should be also considered.

Among the patients in the present series, the rate of patients with elevated prethoracotomy serum CEA levels was 45%, including 23 patients (23%) with borderline levels and 22 (22%) with high levels. In the other reports, this rate varied from 40% to 55%,[13,20-24] almost similar to that in our series. Nevertheless, the 5-year-survival rates in these reports were 24% to 48%, lower than our surgical results. We initially hypothesized that the 5-year-survival rate depends on the percentage of patients with elevated prethoracotomy serum CEA level to the total patients, but the data did not support this hypothesis. This discrepancy could not be clearly explained, but might be due to the difference in patients' backgrounds among surgical centers. In any case, it was commonly accepted that patients with elevated prethoracotomy serum CEA levels showed a poor prognosis among these reports.

We conclude that the prethoracotomy serum CEA level in patients with pulmonary metastases from colorectal cancer is the most important prognostic marker when planning the surgical strategy in such patients. Patients with elevated serum CEA level should undergo a careful prethoracotomy systemic survey and postthoracotomy follow-up for extrathoracic, metastases, in particular brain metastases, and an appropriate combined therapeutic modality should be considered.

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REFERENCES

1. Pogrebniak HW, Pass HI. Initial and reoperative pulmonary metastasectomy: Indications, technique, and results. Semin Surg Oncol 1993; 9: 142–9.
2. Rusch VW. Pulmonary metastasectomy: current indications. Chest 1995; 107(Suppl): 322S–32S.
3. Groeger AM, Kandioler D, Mueller MR, End A, Eckersberger F, Wolner E. Survival after surgical treatment of recurrent pulmonary metastases. Eur J Cardithoracic Surg 1997; 12: 703–5.
4. Pastorino U, Buyse M, Friedel G, Ginsgerg RJ, Girard P, Goldstraw P, et al. Long-term results of lung metastasectomy: Prognostic analyses based on 5206 cases. J Thorac Cardiovasc Surg 1997; 113: 37–49.
5. Zwischenberger JB, Alpard SK. Pulmonary metastasectomy. Ann Thorac Surg 1999; 68: 287–8.
6. Kodama K, Doi O, Higashiyama M, Tatsuta M, Iwanaga T. Surgical management of lung metastases: usefulness of resection with the neodymium: yttrium-aluminium-garnet laser with median sternotomy. J Thorac Cardiovasc Surg 1991; 101: 901–8.
7. Kodama K, Doi O, Higashiyama M, Yokouchi H, Kuriyama K. Surgical treatment of metastatic lung tumors: Recent changes in techniques and indications. Surg Today 1997; 27: 1123–30.
8. Higashiyama M, Kodama K, Takami K, Higaki N, Yokouchi H, Nakayama T, et al. Intraoperative lavage cytologic analysis of surgical margins as a predictor of local recurrence in pulmonary metastasectomy. Arch Surg 2002; 137: 469–74.
9. Wilking N, Petrelli NJ, Herrera L, Regal A-M, Mittelman A. Surgical resection of pulmonary metastases from colorectal adenocarcinoma. Dis Colon Rectum 1985; 28: 562–4.
10. Mansel JK, Zinsmeister AR, Pairolero PC, Jett JR. Pulmonary resection of metastatic colorectal adenocarcinoma: A ten year experience. Chest 1986; 89: 109–12.
11. Goya T, Miyazawa N, Kondo H, Tsuchiya R, Naruke T, Suemasu K. Surgical resection of pulmonary metastases from colorectal cancer: Ten-year follow-up. Cancer 1989; 64: 1418–21.
12. Sauter ER, Bolton JS, Willis GW, Farr GH, Sardi A. Improved survival after pulmonary resection of metastatic colorectal carcinoma. J Surg Oncol 1990; 43: 135–8.
13. McAfee MK, Allen MS, Trastek VF, Ilstrup DM, Deschamps C, Pairolero PC. Colorectal lung metastases results of surgical excision. Ann Thorac Surg 1992; 53: 780–5.
14. McCormack PM, Burt ME, Bains MS, Martini N,

Rusch VW, Ginsberg RJ. Lung resection for colorectal metastases. 10-year results. Arch Surg 1992; 127: 1403–6.

15. Yano T, Hara N, Ichinose Y, Yokoyama H, Miura T, Ohta M. Results of pulmonary resection of metastastic colorectal cancer and its application. J Thorac Cardiovasc Surg 1993;106: 875–9.
16. Saclarides TJ, Krueger BL, Szeluga DJ, Warren WH, Faber LP, Economou SG. Thoracotomy for colon and rectal cancer metastases. Dis Colon Rectum 1993; 36: 425–9.
17. Shirouzu K, Isomoto H, Hayashi A, Nagamatsu Y, Kakegawa T. Surgical treatment for patients with pulmonary metastases after resection of primary colorectal carcinoma. Cancer 1995; 76: 393–8.
18. Van Halteren HK, van Geel AN, Hart AAM, Zoetmulder FAN. Pulmonary resection for metastases of colorectal origin. Chest 1995; 107: 1526–31.
19. Okumura S, Kondo H, Tsuboi M, Nakayama H, Asamura H, Tsuchiya R, et al. Pulmonary resection for metastatic colorectal cancer: Experiences with 159 patients. J Thorac Cardiovasc Surg 1996; 112: 867–74.
20. Girard P, Ducreux M, Baldeyrou P, Rougier P, Chevalier TL, Bougaran J, et al. Surgery for lung metastases from colorectal cancer: Analysis of prognostic factors. J Clin Oncol 1996; 14: 2047–53.
21. Baron O, Amini M, Duveau D, Despins P, Sagan CA, Mlchaud JL. Surgical resection of pulmonary metastases from colorectal carcinoma: Five-year survival and main prognostic factors. Eur J Cardiothorac Surg 1996; 10: 347–51.
22. Inoue M, Kotake Y, Nakagawa K, Fujiwara K, Fukuhara K, Yasumitsu T. Surgery for pulmonary metastases from colorectal carcinoma. Ann Thorac Surg 2000; 70: 380–3.
23. Sakamoto T, Tsubota N, Iwanaga K, Yuki T, Matsuoka H, Yoshimura M. Pulmonary resection for metastases from colorectal cancer. Chest 2001; 119: 1069–72.
24. Zink S, Kayser G, Gabius H-J, Kayser K. Survival, disease-free interval, and associated tumor features in patients with colon/rectal carcinomas and their resected intra-pulmonary metastases. Eur J Cardiothoracic Surg 2001; 19: 908–13.
25. Gutman M, Fidler IJ. Biology of human colon cancer metastasis. World J Surg 1995; 19: 226–34.