Accuracy of helical computed tomography in the detection of pulmonary colorectal metastases

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Objective: This study assessed the sensitivity of helical computed tomography in the detection of pulmonary metastases in patients with colorectal cancer and the role of video-assisted thoracoscopic surgery in patients with pulmonary metastases.

Methods: A total of 120 operations for pulmonary metastases were performed in 91 patients with colorectal cancer. All patients received an open thoracotomy that allowed full operative inspection and palpation. Clinical data, including the size and number of pulmonary metastasis, were retrospectively collected. The difference in the number of pulmonary metastases as determined by computed tomography scan and surgical findings was determined and analyzed.

Results: Operative findings were consistent with the preoperative computed tomography scan reports in 64 of the 120 operations (53.3%). In 32 operations (26.7%), additional metastatic tumors were identified at open thoracotomy. The sensitivity of helical computed tomography in the detection of colorectal cancer metastatic lesions ranged from 35.5% to 95.5%. Unilateral solitary lesion demonstrated on computed tomography scan was an independent factor for the prediction of additional metastatic lesions ($P = .023$).

Conclusions: The sensitivity of helical computed tomography scan in the detection of pulmonary metastases can reach 95.5% in patients with colorectal cancer with a solitary metastatic lesion. A unilateral solitary lesion demonstrated on preoperative computed tomography scan is an independent factor for prediction of additional metastatic lesions. If feasible, video-assisted thoracoscopic surgery may be justified in patients with colorectal cancer with solitary pulmonary metastases. (*J Thorac Cardiovasc Surg* 2011;141:1207-12)

Colorectal cancer (CRC) is a leading cause of cancer-related mortality worldwide. After curative resection for CRC, distant metastases to the liver or lungs inevitably will develop in more than 10% of patients.¹ An aggressive, multidisciplinary approach including surgical resection is recommended for recurrent CRC.^{2,3} Numerous studies have emphasized the role of surgical resection for pulmonary metastases from CRC and concluded that certain factors, including lymph node metastases, serum carcinoembryonic antigen (CEA) level, number and size of pulmonary metastases, disease-free interval, and resectability, are related to surgical outcome.⁴⁻⁹ Although the majority of studies have concluded that surgery for

pulmonary metastases from CRC can improve long-term survival and obtain better local control, some authors^{9,10} have argued that the retrospective nature of these studies does not allow definitive conclusions. Instead, they suggested a prospective trial should be undertaken whenever feasible.^{9,10}

The number of metastases demonstrated by chest computed tomography (CT) is frequently used as a prognostic factor, because CT findings are important in deciding whether complete resection of pulmonary metastases can be carried out. Some authors suggest the sensitivity of a CT scan to be insufficient, and that complete manual exploration during thoracotomy should be considered for patients undergoing pulmonary metastasectomy.^{11,12} A 2004 study reported that the sensitivity of helical CT in the detection of pulmonary metastases was only 78%, and concluded that despite the use of helical CT, palpation of the lung is still necessary.¹² In contrast, another recent study suggested that palpation is not mandatory, and the application of multi-detector CT in conjunction with video-assisted thoracoscopic surgery (VATS) is appropriate for metastasectomy.¹³

The use of VATS in the resection of pulmonary metastases is debatable. Potential advantages of the minimally invasive approach include smaller incisions, less postoperative pain, and shorter hospitalization. However, some disadvantages include difficulty localizing central tumors and the possible exclusion of small lesions undetected by CT scan, which could influence patient outcome.¹⁴ This

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Abbreviations and Acronyms

CEA	= carcinoembryonic antigen
CRC	= colorectal cancer
CT	= computed tomography
VATS	= video-assisted thoracoscopic surgery

study assessed the accuracy of preoperative helical CT scanning in patients with CRC with pulmonary metastases and the role of VATS in these patients.

PATIENTS AND METHODS**Patients**

From January 2000 to December 2009, 153 pulmonary metastasectomies were performed in 120 patients with CRC at Taipei Veterans General Hospital. The institutional review board of Taipei Veterans General Hospital approved this study and granted an exemption from informed consent on August 26, 2010 (201008231C). All patients received a current-generation scanner, a 64-detector row CT scanner (Toshiba Aquilion 64 CT Scanner; Toshiba Medical Systems Corp, Tochigi, Japan). The images were reconstructed at intervals of 5 mm. Of these 120 patients, 91 who received an open thoracotomy that allowed a full inspection and palpation were enrolled in the study. In total, 120 operations were performed in these 91 patients. Patients who had VATS or a vertical mini-thoracotomy were excluded from the study because complete manual palpation is difficult in these patients. Two patients had unresectable disease due to great vessel invasion. These 2 patients were also excluded from the analysis because the exact number of pulmonary metastases could not be ascertained. Seven patients with CRC had thoracotomy and pulmonary resection for suspected metastatic lesions, which proved to be benign. These 7 patients were excluded from the analysis. The preoperative workup included physical examination, chest radiograph, helical chest CT scan (5-mm cut), pulmonary function testing, CEA level, flexible colonoscopy, abdominal CT scan to rule out local recurrence, and radionuclide bone scan to rule out bone metastases. Positron emission tomography scan was not routinely used in the preoperative workup strategy because the health insurance did not cover the expense in this group of patients in the country. The criteria for resection included primary tumor under control (ie, no local recurrence of primary CRC), no extrapulmonary metastases, medically stable for surgery, and the possibility of complete resection based on the CT scan findings. The laterality and number of pulmonary nodules on the CT scan during the preoperative study were reevaluated by 1 chest surgeon and a radiologist with specialized training in reading chest CT images (M-H.W). Patient demographic data were retrospectively collected. The difference in the number of pulmonary metastases as determined by interpretation of the preoperative CT scan and on the final pathologic report was analyzed.

Statistical Analyses

The chi-square test was used to compare the data between the subgroups. Multivariate analysis adjusted for confounding factors was performed using the Cox regression model and the forward stepwise method, incorporating all variables found to be significant in univariate analysis. Factors related to additional malignant lesion were analyzed with logistic binary regression. All calculations were performed using the Statistical Package for the Social Sciences, version 12.0 (SPSS, Inc, Chicago, Ill).

RESULTS**Patient Demographic and Operative Data**

The demographic data of the 91 patients are shown in Table 1. There were 59 male patients (65%) and 32 female

patients (35%) with a mean age of 65.0 years (range, 36–89 years). The primary carcinoma was located in the colon in 54 patients (59%) and in the rectum in 37 patients (41%). The mean disease-free interval (interval between resection of the primary tumor and the diagnosis of lung metastases) was 33.5 months (range, 0–192 months; median, 24 months). Sixty-eight patients (74.6%) received a unilateral thoracotomy, including 6 patients who received a re-thoracotomy for pulmonary metastasis. Five patients (5.5%) underwent a synchronous bilateral thoracotomy for bilateral lung metastases, and 18 patients (19.8%) underwent a staged bilateral thoracotomy for bilateral lung metastasis. Of these 18 patients, 5 (5.5%) received bilateral thoracotomies when contralateral lung metastases were subsequently discovered. There were no operative or in-hospital mortalities and major morbidity. Operative data are summarized in Table 2. The maximum number of pulmonary nodules on the CT scan in our study was 20. In 2 patients having pneumonectomy for pulmonary metastases, the lesions were large and centrally located. One patient had 1 lesion, and 1 patient had 2 lesions. There were no extra nodules identified in these 2 cases. In patients undergoing lobectomy, 17 of 21 had solitary lesion (80.9%). Only 1 patient had extra nodules in the same lobe (4.7%). The CEA level was elevated in 46 of 120 operations (cutoff value, ≤ 6.0 ng/mL). The mean size of the tumor removed was 2.68 cm (range, 0.3–9.0 cm).

Possibility of Additional Benign and Metastatic Lesions Found during Surgery

The results of the univariate analysis of the possibility of additional benign and metastatic lesions found during the 120 operations are shown in Tables 3 and 4. The operative findings were consistent with the preoperative CT scan reports in 64 operations (53.3%). In 24 operations (20%), additional benign lesions were found at thoracotomy. A total of 57 of 368 pulmonary lesions (15.4%) resected were benign. Patients with unilateral and solitary lung lesion on preoperative chest CT scan were more likely to have additional benign lung lesions ($P = .043$). In 32 of the 120 operations (26.7%), additional malignant tumors were identified at open thoracotomy. Patients with Dukes' stage C and D, disease-free interval less than 36 months, elevated preoperative CEA level, and suspected bilateral or multiple metastatic lesions demonstrated on preoperative chest CT scan were found to have more malignant metastatic lesions during their operations than indicated by CT scan. The sensitivity in detection of pulmonary metastasis varied from 35.5% to 95.5%. For patients with 1 to 3 nodules (108 operations) on preoperative CT scan, disease-free interval, tumor number, and laterality on CT are still significant predictive factors for additional malignant lesions. The results of the multivariate analysis of the possibility of additional malignant lesion are shown in Table 5.

TABLE 1. Characteristics of the 91 patients with colorectal cancer and pulmonary metastases

Demographics	No. (%)
Age, mean (range)	65.02 y (36–89)
<65 y	40 (44%)
≥65 y	51 (56%)
Gender	
Male	59 (65%)
Female	32 (35%)
Site of primary tumor	
Colon	54 (59%)
Rectum	37 (41%)
Grade of primary tumor	
Dukes' A	9 (10%)
Dukes' B	29 (32%)
Dukes' C	40 (44%)
Dukes' D	13 (14%)
Appearance of metastasis	
Synchronous	10 (11%)
Metachronous	81 (89%)
Disease-free interval, mean (range)	33.47 mo (0–192)
<36 mo	56 (61.5%)
≥36 mo	35 (38.5%)
Approaches	
Unilateral thoracotomy	68 (74.6%)
Synchronous bilateral thoracotomy	5 (5.5%)
Bilateral thoracotomy	18 (19.8%)

A unilateral solitary lesion revealed on preoperative chest CT scan was an independent factor for the prediction of additional malignant metastatic lesions compared with the other factors.

DISCUSSION

The prognosis of patients with CRC is determined by local or distant recurrence after resection of the primary tumor. For patients with pulmonary metastases, significant prognostic factors are reported to include tumor resectability, tumor stage, number of pulmonary metastases, size of metastases, laterality of metastases, resection margin, hilar or mediastinal lymph node metastases, disease-free interval, and pre-thoracotomy serum CEA level.¹⁻⁸ Helical CT scan is the primary diagnostic tool used to detect pulmonary metastases and quantify the tumor number and size and identify location. The literature concerning the accuracy and sensitivity of a preoperative CT scan in the detection of pulmonary metastases in patients with CRC is limited. The results of this study indicated that the sensitivity of CT in the detection of pulmonary metastatic lesions in patients with CRC varied from 35.5% to 95.5%. Patients with an early-stage primary tumor (especially Dukes' A), disease-free interval more than 36 months, normal pre-thoracotomy CEA level, and unilateral solitary metastasis were likely to have fewer additional metastatic lesions. These factors are also favorable prognostic factors accord-

TABLE 2. Features of the 120 pulmonary metastasectomies in 91 patients with colorectal cancer

Demographics	No. (%)
No. of lesions on CT	
1	65 (54.2%)
2	34 (28.3%)
3	9 (7.5%)
≥4	12 (10%)
Laterality on CT	
Unilateral	68 (56.7%)
Solitary	44
Multiple	24
Bilateral	52 (43.3%)
Solitary	21
Multiple	31
Pre-thoracotomy serum CEA level	
Normal	74 (61.7%)
Elevated	46 (85.1%)
No. of metastatic lesion resected	
1	63 (52.5%)
2	29 (24.2%)
3	8 (6.7%)
≥4	20 (16.7%)
Tumor size, mean (range)	2.68 cm (0.3–9.0)
≤3 cm	68 (56.7%)
>3 cm	52 (43.3%)
Operative procedures	
Wedge resection	97 (80.8%)
Lobectomy	21 (17.5%)
Pneumonectomy	2 (1.7%)

CT, Computed tomography; CEA, carcinoembryonic antigen.

ing to reports in the literature.^{1,2,4} We assume that fewer additional metastatic lesions found during surgery in these patients may indicate relatively benign tumor behavior and a low occult metastasis rate. Some previous studies also recommended that VATS can be used in patients with early-stage and fewer metastases.^{15,16}

The traditional principle for resection of pulmonary metastases is to completely remove all the metastatic lesions detected by CT scan if possible. Open thoracotomy is thus recommended as the procedure of choice, because only manual palpation during surgery can ensure removal of all metastatic lesions, which is the limitation of VATS.^{17,18} However, some authors have suggested that the use of VATS does not result in inferior overall survival compared with thoracotomy in patients with CRC with pulmonary metastases.^{15,16,19} This study carefully examined the patients undergoing open thoracotomy for pulmonary metastases from CRC and focused on the accuracy of detection of metastatic lesions by use of the CT scan in conjunction with thorough palpation during surgery. The overall detection rate of additional metastatic lesions was 26.7% at open thoracotomy. We observed that additional metastatic lesions were found in 2 of 44 thoracotomies (4.5%) in patients with unilateral solitary

TABLE 3. Univariate analysis of the possibility of additional benign lesions

Demographics	No. (%)	Additional benign (%)	P value
Age			.314
<65 y	56 (46.7%)	9 (16.1%)	
≥65 y	64 (53.3%)	15 (23.4%)	
Gender			.925
Male	76 (63.3%)	15 (19.7%)	
Female	44 (36.7%)	9 (20.5%)	
Site of primary tumor			1.00
Colon	70 (58.3%)	14 (20.0%)	
Rectum	50 (41.7%)	10 (20.0%)	
Grade of primary tumor			.307
Dukes' A and B	49 (40.8%)	12 (24.5%)	
Dukes' C and D	71 (59.2%)	12 (16.9%)	
Disease-free interval			.849
<36 mo	77 (64.2%)	15 (19.5%)	
≥36 mo	43 (35.8%)	9 (20.9%)	
Pre-thoracotomy CEA level			.925
Within normal	74 (61.7%)	15 (20.3%)	
Elevated	46 (38.3%)	9 (19.6%)	
Tumor number on CT			.051
1	65 (54.2%)	18 (27.7%)	
2	34 (28.3%)	6 (17.6%)	
3	9 (7.5%)	0 (0%)	
≥4	12 (10.0%)	0 (0%)	
Tumor laterality on CT			.043*
Unilateral	68 (56.7%)	18 (26.5%)	
Bilateral	52 (43.3%)	6 (11.5%)	
Tumor laterality and number on CT			.043*
Unilateral solitary	44 (36.7%)	13 (29.5%)	
Unilateral multiple	24 (20.0%)	5 (20.8%)	
Bilateral solitary	21 (17.5%)	5 (23.8%)	
Bilateral multiple	31 (25.8%)	1 (3.2%)	
Tumor size			.598
≤3 cm	90 (75.0%)	19 (21.1%)	
>3 cm	30 (25.0%)	5 (16.7%)	
Operative methods			.132
Wedge resection	97 (80.8%)	22 (22.7%)	
Anatomic resection	23 (19.2%)	2 (8.7%)	

CT, Computed tomography; CEA, carcinoembryonic antigen. * $P < .05$ was considered significant by chi-square test.

lesions demonstrated by a preoperative CT scan, which was significantly lower than in patients with multiple or bilateral lesions as revealed by CT scan. Age, gender, and site of the primary tumor were not correlated with the detection rate of additional metastatic lesions. Kayton and colleagues²⁰ reported that only an approximate correlation exists between CT findings and the number of lesions identified at thoracotomy in cases of pulmonary metastases from osteosarcoma. The authors suggested that minimal access procedures should not be the approach of choice in these patients. Another study also reported that helical CT scans miss metastases in more than 40% of cases of pulmonary metastases

from various origins.¹² In a prospective study that enrolled 166 patients with lung cancer undergoing lung resection via thoracotomy, additional malignant lesions that were not detected by preoperative CT scans, and which could possibly be missed by VATS, were identified in 14 patients (8.4%).²¹ In contrast, another study of 102 patients with CRC with pulmonary metastases found that the ability to detect pulmonary metastases was limited by preoperative CT scan and surgical techniques. The authors concluded that finger palpation for detecting additional pulmonary nodules at metastasectomy might play only a limited role in improving the postoperative outcome of patients with pulmonary metastasis from CRC, especially when the pulmonary lesions are small.²²

There are 3 issues to consider for patients with pulmonary metastases revealed by CT scan. The first is whether the sensitivity of a CT scan is sufficient. The second is whether the surgeon can identify all the metastatic lesions via open thoracotomy in every operation by use of a finger palpation. The third is whether complete removal of all metastatic lesions is possible when many lesions are present and whether a patient's prognosis is improved by their removal. With the evolution of CT scanning technology, helical CT scanning can detect smaller pulmonary nodules than older technology.²³ In this study, standard-dose helical CT scan was used in all patients for screening of pulmonary metastases. According to the results from Margaritora and colleagues,¹¹ the sensitivity of helical CT is better than high-resolution CT (82.1% vs 75%), possibly because there is a 10-mm gap in high resolution CT. High-resolution CT is to assess a generalized lung disease with 1-mm thick images taken at 10-mm spacings. It is unsuitable for assessment of lung cancer or other localized lung disease. There are also some differences between standard-dose CT and low-dose CT. The radiation dose of low-dose CT can be reduced to approximately 10% to 20% of standard-dose CT (~0.3–0.55 mSv vs 3–27 mSv), which is acceptable for repeat examination. In addition, low-dose CT can be completed in a single breath-hold without contrast medium injection, which can avoid the risk of anaphylaxis and acute renal failure. However, the number of pulmonary nodules detected by low-dose CT was significantly less than those detected by standard-dose CT, especially for nodules smaller than 5 mm. Even with improvements in CT scanning, the question remains whether the use of VATS is justified in treating pulmonary metastases from CRC. A 2008 study concluded that there was significant difference in the survival of patients with CRC with pulmonary metastases who underwent thoracotomy or thoracoscopy.²⁴ In contrast, a 2009 study that reported an 11-year experience of resection of pulmonary metastases suggested that VATS is inferior to conventional open thoracotomy and was not recommended as a standard procedure.²⁵ Some authors have advocated that VATS can be

TABLE 4. Univariate analysis of the possibility of additional malignant lesions and sensitivity of preoperative computed tomography scan

Demographics	No. (%)	Additional malignant (%)	Sensitivity of CT scan (%)	P value
Age				.204
<65 y	56 (46.7%)	18 (32.1%)	67.9%	
≥65 y	64 (53.3%)	14 (21.9%)	78.1%	
Gender				.162
Male	76 (63.3%)	17 (22.4%)	77.6%	
Female	44 (36.7%)	15 (34.1%)	65.9%	
Site of primary tumor				.485
Colon	70 (58.3%)	17(24.3%)	75.7%	
Rectum	50 (41.7%)	15 (30.0%)	70%	
Grade of primary tumor				.011*
Dukes' A and B	49 (40.8%)	7 (14.3%)	85.7%	
Dukes' C and D	71 (59.2%)	25 (35.2%)	64.8%	
Disease-free interval				.001*
<36 mo	77 (64.2%)	28 (36.4%)	63.6%	
≥36 mo	43 (35.8%)	4 (9.3%)	90.7%	
Pre-thoracotomy CEA level				.015*
Within normal	74 (61.7%)	14 (18.9%)	81.1%	
Elevated	46 (38.3%)	18 (39.1%)	60.9%	
Tumor number on CT				<.001*
1	65 (54.2%)	6 (9.2%)	90.8%	
2	34 (28.3%)	10 (29.4%)	70.6%	
3	9 (7.5%)	4 (44.4%)	55.6%	
≥4	12 (10.0%)	12 (100%)	0%	
Tumor laterality on CT				<.001*
Unilateral	68 (56.7%)	8 (11.7%)	88.3%	
Bilateral	52 (43.3%)	24 (46.2%)	53.8%	
Tumor laterality and number on CT				<.001*
Unilateral solitary	44 (36.7%)	2 (4.5%)	95.5%	
Unilateral multiple	24 (20.0%)	6 (25.0%)	75.0%	
Bilateral solitary	21 (17.5%)	4 (19.0%)	81.0%	
Bilateral multiple	31 (25.8%)	20 (64.5%)	35.5%	
Tumor size				1.00
≤3 cm	90 (75.0%)	24 (26.7%)	73.3%	
>3 cm	30 (25.0%)	8 (26.7%)	73.3%	
Operative methods				.263
Wedge resection	97 (80.8%)	28 (28.9%)	71.1%	
Anatomic resection	23 (19.2%)	4 (17.4%)	82.6%	

CT, Computed tomography; CEA, carcinoembryonic antigen. *P < .05 was considered significant by chi-square test.

used as an acceptable alternative in selected patients with small pulmonary metastases, fewer nodules, and peripheral lesions.^{15,16} However, for patients with deeply located metastatic lesions, it would be difficult to identify or resect the lesions by VATS. In this study, CT scan sensitivity is approximately 95% in patients with only 1 metastatic lesion in lungs. For patients with multiple metastases in 1 or both lungs, however, the sensitivity of CT scanning is poor. We consider that multiple pulmonary metastases indicated advanced disease. More occult metastatic lesions were possibly missed on CT scan. This study found that the sensitivity of CT scan in patients with more than 3 pulmonary lesions or bilateral multiple lesions was even poorer. The sensitivity of the CT scanning was not influenced by the tumor size. The

present results indicate that VATS may be feasible and justified in patients with CRC with solitary pulmonary metastases. However, even with high sensitivity of CT scan, for patients with unilateral solitary lesion, there was still a 5% or greater chance that additional malignant lesions could be missed if the patients underwent VATS.

Study Limitations

This study has several limitations to consider. First, all the data were retrospectively collected. Although the CT scan images were reviewed by 1 chest surgeon and 1 specialized radiologist, the operative findings were recorded according to the operative and pathologic reports. Some bias might exist, such as the involvement of different surgeons over the time of the study. For example, results of

GTS

TABLE 5. Multivariate analysis of the possibility of additional malignant lesions

Variable	OR	95% CI	P value
Grade of primary tumor			
Dukes' A and B	1		
Dukes' C and D	2.311	0.748–7.133	.145
Disease-free interval			
≤36 mo	1		
>36 mo	3.356	0.084–1.063	.062
Pre-thoracotomy CEA level			
Normal	1		
Elevated (>6 ng/mL)	2.372	0.854–6.586	.097
Tumor laterality and number on CT			
Unilateral solitary	1		
Unilateral multiple	9.010	1.325–44.867	.023*
Bilateral solitary	7.349	0.907–37.009	.063
Bilateral multiple	33.665	5.415–144.207	<.001*

OR, Odds ratio; CI, confidence interval; CT, computed tomography; CEA, carcinoembryonic antigen. Multivariate analysis was performed using the Cox regression model. * $P < .05$ was considered significant.

finger palpation or the findings of additional metastatic lesions may not be consistent in all cases. Second, we looked only at the relationship between preoperative CT images and operative findings, and investigated whether demographic data would influence the detection rates of additional pulmonary metastatic lesions. We did not follow up the patients in the postoperative period to see whether early recurrence was more likely to develop in patients with multiple pulmonary metastases. Long-term follow-up or a prospective trial may be required to evaluate the effectiveness of helical CT scan in the detection of pulmonary metastases in patients with CRC and appropriate indications for VATS in these patients.

CONCLUSIONS

The sensitivity of helical CT scanning in detection of pulmonary metastases can reach 95% in patients with CRC with unilateral solitary metastatic lesion. With thorough palpation during surgery, patients with early-stage disease (especially Dukes' A), disease-free interval more than 36 months, normal pre-thoracotomy CEA level, and unilateral solitary metastases were likely to have fewer additional metastatic lesions. Unilateral solitary lesion demonstrated on a preoperative CT scan is an independent factor for prediction of additional metastatic lesions. We suggest that VATS is justified in patients with CRC with unilateral solitary pulmonary metastasis, if feasible.

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