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Clinical Research

Surgical Strategy for Primary Colorectal Carcinoma and Synchronous Pulmonary Metastasis Resection

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Background: The surgical strategy for single-stage resection of primary colorectal cancer (CRC) and synchronous pulmonary metastases remains a matter of debate.
Methods: Perioperative data of patients who underwent single-stage resection of primary CRC and synchronous pulmonary metastases were compared to those of patients who underwent 2-stage resections. The demographic data, number of metastases, type of pulmonary and colorectal resections, operation time, blood loss, postoperative complications, morbidities, mortality, medical costs, and length of hospital stay were analyzed.
Results: Twenty-two patients underwent single-stage resection of primary CRC and pulmonary metastases, while 27 patients underwent 2-stage resection. Tumor size and the number of pulmonary metastases were not significantly different between the 2 groups. The extent of pulmonary metastasectomy and abdominal procedures were similar in both groups, as was the thoracic surgical approach (video-assisted thoracic surgery vs. thoracotomy). However, open laparotomy was performed more frequently in the 2-stage group than in the single-stage group (p=0.045), which also had a longer total anesthetic time (p=0.013). The operation time, medical costs, estimated blood loss, complication rates, and severity were similar in both groups, but the length of hospital stay was shorter in the single-stage group (p<0.001).
Conclusion: Single-stage colorectal and pulmonary resection shortened the overall hospital stay, with no significant changes in operation time, medical costs, hospital mortality, and morbidity. Therefore, single-stage resection could be a good surgical strategy in selected patients.

Keywords: Colorectal neoplasms, Metastasectomy

Introduction

The synchronous presence of lung metastases with colorectal cancer (CRC) generally requires staged resections, such as pulmonary resection after colorectal resection, in 2 different hospitalizations. Both abdominal and thoracic incisions are inevitable even in minimally invasive approaches, such as video-assisted thoracic surgery (VATS). Therefore, surgeons perform staged lung resection due to the possibility of increased morbidity and mortality. However, recent advances in multidisciplinary treatment are changing the surgical approach for these patients. In terms of patient quality of life and cost-effectiveness, single-stage colorectal and pulmonary resection with 1 hospitalization and 1 induction of anesthesia might be preferable. Therefore, Samsung Medical Center has offered single-stage surgical resection of CRC and pulmonary metastases to selected patients since 2008.

Our strategy in metastatic CRC is to offer surgery rather than chemotherapy, as long as resectability and operability are ensured, when pulmonary resection is expected to be relatively simple and short for relatively young patients (<65 years). The optimal timing for surgical resection of synchronous metastases has been debated and has evolved over time. Referral bias, institutional bias, and patient bias still dictate the timing of surgery in these patients.

To the best of our knowledge, the safety of the single-stage approach for CRC with synchronous pulmonary me-

tastasis has been rarely discussed. The aim of this study was to investigate the safety and feasibility of primary CRC and metastatic pulmonary resection in 1 operative session.

Methods

Patients and data collection

Data were retrospectively collected from patients who underwent lung metastasectomy from CRC between March 2004 and April 2014. Among these patients, those who underwent single-stage or 2-stage resection of CRC and pulmonary metastases were included in this study. Single-stage resection (group S) was defined as single-stage colorectal and pulmonary resection in 1 hospitalization and a single induction of anesthesia. Two-stage resection (group T) was defined as colorectal surgery and pulmonary resection in 1 hospitalization with 2 inductions of general anesthesia or in 2 different hospitalizations. However, in the latter case, the time interval between CRC surgery and pulmonary metastasectomy was limited to <2 months.

The decision to perform either single-stage or 2-stage resection was determined via collaboration between colorectal and thoracic surgeons. Ultimately, once it was decided that surgery was indicated, the decision to perform single-stage or 2-stage resection was based on the complexity of pulmonary and colorectal resections and patients' comorbidities. In our institution, no definitive criteria regarding tumor size or depth of lung lesions were used to select patients for single-stage resection. However, we generally tried to offer patients single-stage resection when they had good performance status, no significant comorbidities, were relatively young (<65 years), and when thoracic surgery seemed to be a simple procedure. Otherwise, 2-stage resection was preferred.

Patients' baseline characteristics and treatment modalities were obtained from their medical records. The following parameters were recorded and included in the statistical analysis: sex, age, tumor size, number of resected pulmonary metastases, bilaterality, location of lung lesions (central or peripheral), primary tumor site, thoracic surgical approach (thoracotomy versus VATS), type of thoracic procedure (precision excision, wedge resection, segmentectomy, lobectomy, bilobectomy, or pneumonectomy), abdominal surgical approach (laparoscopy or laparotomy), type of abdominal procedure (hemicolectomy, low anterior resection, or abdominoperineal resection), transfusion, estimated blood loss, length of hospital stay, total medical costs, and administration of preoperative or adjuvant chemotherapy. Moreover, the American Society of Anesthesiologists (ASA) physical status classification system was used to assess the fitness of patients in both groups before surgery: I=healthy patient; II=mild systemic disease (no functional limitation); III=severe systemic disease (definite functional limitation); IV=severe systemic disease that is a constant threat to life; V=moribund patient unlikely to survive 24 hours with or without operation.

Medical costs were analyzed by comparing the total hospital costs between the two groups, including the costs of the operation, materials, medicines, bed charges, and nursing care. This study was approved by the Institutional Review Board of Samsung Medical Center which waived the requirement for informed patient consent due to its retrospective nature (IRB approval no., SMC 2021-09-068).

Statistical analysis

For the comparison of continuous and categorical variables, the Mann-Whitney U test, chi-square test, or Fisher exact test was used as appropriate. The reported data are expressed as mean±standard deviation or median (range), and differences between means were tested using the Student t-test. All p-values <0.05 were considered to indicate statistical significance. All statistical analyses were performed using JMP ver. 12.1 (SAS Institute Inc., Cary, NC, USA).

Results

Patient demographics

A total of 55 patients underwent pulmonary metastasectomy with curative intent for CRC between March 2004 and April 2014. Forty-nine of these patients were enrolled in this study. Six patients were excluded due to incomplete information because they underwent abdominal surgery at a different hospital. All patients were confirmed to have synchronous CRC with pulmonary metastasis based on the final pathologic diagnosis. There were 28 and 21 primary cancers in the colon (57.1%) and rectum (42.9%), respectively. Of the 49 patients, 11 (22.5%) received neoadjuvant chemotherapy, and 37 (75.5%) received adjuvant chemotherapy. Patient characteristics according to surgical strategy (single-stage versus 2-stage) are summarized in Table 1. Twenty-two patients underwent simultaneous resection of CRC and pulmonary metastasis in a single-stage resection procedure; 27 patients underwent 2-stage resection. The median patient age at the time of pulmonary metastasecto-

Table 1. Patient characteristics in the 2-stage and single-stage resection groups

Characteristic	All patients (N=49)	Group T (N=27)	Group S (N=22)	p-value
Age (yr)	61 (29–82)	65 (37–82)	58 (29–68)	0.003
≤65		14	19	
>65		13	3	
Sex				0.445
Male	23 (47.0)	14 (51.9)	9 (40.9)	
Female	26 (53.0)	13 (48.1)	13 (59.1)	
American Society of Anesthesiologists class				0.973
1	7 (14.3)	4 (14.8)	3 (13.6)	
2	38 (77.6)	21 (77.8)	17 (77.3)	
3	4 (8.1)	2 (7.4)	2 (9.1)	
Location of primary colorectal cancer				0.438
Colon	28 (57.1)	17 (63.0)	11 (50.0)	
Rectum	21 (42.9)	10 (37.0)	11 (50.0)	
Surgical approach for colorectal cancer				0.045
Minimally invasive surgery laparoscopy	25 (51.0)	10 (37.0)	15 (68.2)	
Laparotomy	24 (49.0)	17 (63.0)	7 (31.8)	
Primary resection				0.405
Right hemicolectomy	3 (6.1)	3 (11.1)	0	
Left hemicolectomy	2 (4.1)	1 (3.7)	1 (4.6)	
Low anterior resection	25 (51.0)	13 (48.2)	12 (54.6)	
Abdominoperineal resection	19 (38.8)	10 (37.0)	9 (40.9)	
Preoperative chemotherapy	11 (22.5)	4 (14.8)	7 (31.8)	0.379
Adjuvant chemotherapy	37 (75.5)	20 (74.1)	17 (77.2)	0.796
Surgical approach for pulmonary lesions				0.216
Video-assisted thoracic surgery	36 (73.5)	18 (66.7)	18 (81.8)	
Thoracotomy	13 (26.5)	9 (33.3)	4 (18.2)	
Extent of pulmonary resection				0.508
Precision excision	1 (2.0)	1 (3.7)	0	
Wedge resection	33 (67.3)	17 (62.9)	16 (72.7)	
Segmentectomy	6 (12.2)	5 (18.5)	1 (4.6)	
Lobectomy	9 (18.4)	4 (14.8)	5 (22.7)	

Values are presented as median (range), number, or number (%).
Group T, 2-stage resection group; group S, single-stage resection group.

my was 61 years (range, 29–82 years), and 23 patients (46.9%) were men. Group S (median age, 58 years) was younger than group T (median, 65 years). Based on the ASA classification, more than 91% of patients were classified as ASA I or II. Only four patients (8.1%) were classified as ASA III. There were no statistically significant differences in the proportion of ASA classes between the 2 groups (Table 1).

Characteristics of pulmonary metastasis

The characteristics of pulmonary metastasis are summarized in Table 2. The mean number of lung metastases was 1.41±0.81. The mean number of metastases in groups T and S was 1.22±0.67 and 1.63±1.05, respectively (p=0.100). The mean size of the largest pulmonary nodule was 1.66±1.04 cm. There was no significant difference in tumor size between the two groups (p=0.717). Of the 49 patients, 13 (26.5%) had multiple pulmonary metastases, and 7 (14.3%) had bilateral pulmonary lesions. The pulmonary metastases in most cases were located in peripheral areas (n=33, 67.3%) rather than in central areas (n=16, 32.7%). However, there was no association between pulmonary tumor location (central versus peripheral) and surgical strategy (single-stage versus 2-stage) (p=0.549).

Surgical approach

The surgical extent of the abdominal and thoracic procedures is summarized in Table 1. Most of the abdominal procedures were performed using low anterior resection (n=25, 51.0%), followed by abdominoperineal resection

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Table 2. Surgical management and pathologic findings in the 2-stage and single-stage resection groups

Characteristic	All patients (N=49)	Group T (N=27)	Group S (N=22)	p-value
No. of lung metastases	1.41±0.81	1.22±0.67	1.63±1.05	0.100
Multiple pulmonary metastases	13 (26.5)	5 (18.5)	8 (36.4)	0.159
Maximum tumor size	1.66±1.04	1.70±0.96	1.60±1.15	0.717
Bilaterality	7 (14.3)	2 (7.4)	5 (22.7)	0.127
Location of the pulmonary lesions				0.549
Central	16 (32.7)	10 (37.0)	6 (27.3)	
Peripheral	33 (67.3)	17 (63.0)	16 (72.7)	

Values are presented as mean±standard deviation or number (%).
Group T, 2-stage resection group; group S, single-stage resection group.

Table 3. Postoperative outcomes in the 2-stage and single-stage resection groups

Variable	All patients (N=49)	Group T (N=27)	Group S (N=22)	p-value
Total anesthetic time (min)	346 (150–801)	389 (224–801)	321 (150–540)	0.013
Total operation time (min)[a]	285 (125–711)	280 (125–711)	321 (150–540)	0.529
Thoracic operation time (min)	90 (33–230)	96 (33–224)	80.5 (40–230)	0.779
Abdominal operation time (min)	170 (79–488)	188 (90–448)	166.5 (79–350)	0.447
Estimated blood loss (mL)	200 (50–950)	200 (50–950)	200 (50–500)	0.743
Perioperative transfusion	1 (1.8)	0	1 (4.5)	NS
Length of stay (day)	11 (6–25)	14 (8–25)	7.5 (6–19)	<0.001
Time interval between thoracic and abdominal operation (day)	12 (0–58)	38 (4–58)	0	NS
Total medical cost (USD)[b]	13,415 (8,499–25,919)	13,918 (9,092–24,326)	12,447 (8,499–25,919)	0.273

Values are presented as median (range) or number (%).
Group T, 2-stage resection group; group S, single-stage resection group; NS, not significant; KRW, Korean won; USD, US dollar.
[a]Total operation time (min)=thoracic operation time+abdominal operation time. [b]Exchange rate from KRW to USD: 1.00 USD=1,120 KRW.

(n=19, 38.8%), right hemicolectomy (n=3, 6.1%), and left hemicolectomy (n=2, 4.1%). With regard to the abdominal surgical approaches, 25 patients (51.0%) underwent laparoscopy, while 24 patients (49.0%) had laparotomy. Most operations for pulmonary metastases were performed using wedge resection (n=33, 67.3%), followed by lobectomy (n=9, 18.4%), segmentectomy (n=6, 12.2%), and precision excision (n=1, 2.0%). With regard to the thoracic surgical approaches, 36 patients (73.4%) underwent VATS, while 13 patients (26.5%) underwent thoracotomy. There were no significant differences between the 2 groups in terms of the surgical extent of abdominal and thoracic procedures. However, open laparotomy was performed more frequently in group T (n=17, 63.0%) than in group S (n=7, 31.8%) (p=0.045).

Postoperative outcomes in the 2-stage versus single-stage group (group T versus group S)

Postoperative outcomes are summarized in Table 3. The median total operation time, including the abdominal and thoracic procedures, was 285 minutes (range, 25–711 minutes). In group T, the total anesthesia time was longer than that in group S (p=0.011). The median length of hospital stay was 11 days (range, 6–25 days), and it was shorter in group S (median, 7.5 days) than in group T (median, 14 days) (p<0.001). Only 1 patient (1.8%) who underwent single-stage resection required perioperative transfusion. The median estimated blood loss was 200 mL (50–950 mL). There was no significant difference in the estimated blood loss between the 2 groups. The median total medical cost was 13,415 US dollars (USD) (range, 8,499–25,919 USD). There was no significant difference in the total medical cost between group T (13,918 USD) and group S (12,447 USD) (p=0.273).

Complications after colorectal and pulmonary resection in both groups

Postoperative complications are summarized in Table 4. There was no postoperative mortality in either group. Among the 49 patients, 11 (22.4%) had postoperative com-

Table 4. Postoperative complications in the 2-stage and single-stage resection groups

Variable	All patients (N=49)	Group T (N=27)	Group S (N=22)	p-value
Complications				0.518
Yes	11 (22.4)	7 (25.9)	4 (18.2)	
No	38 (77.6)	20 (74.1)	18 (81.8)	
Most severe grade of complications				0.119
Grade 1 and 2	6 (10.9)	5 (18.5)	1 (4.5)	
Grade 3 and 4	5 (9.1)	2 (7.4)	3 (13.6)	
Grade 5	0	0	0	
Mortality within 90 days	0	0	0	
Abdominal procedure-related complications	4 (7.3)	2 (7.4)	2 (9.1)	0.831
Thoracic procedure-related complications	7 (12.7)	5 (18.5)	2 (9.1)	0.348

Values are presented as number (%).
Group T, 2-stage resection group; group S, single-stage resection group.

plications. According to the Clavien–Dindo classification, 5 patients (10.2%) had grade 1 or 2 complications, and 5 (10.2%) had grade 3 or 4. Four patients (8.2%) had abdominal procedure-related complications, which included laparotomy wound infection (n=1), intraoperative bladder injury (n=1), urinary tract infection (n=1), and postoperative ileus (n=1). Seven patients (14.3%) had thoracic procedure-related complications, including prolonged air leak (n=4), postoperative pneumothorax (n=2), and arrhythmia (n=1). There were no statistically significant between-group differences in the amount or severity of morbidity and mortality.

Discussion

Approximately 50%–60% of patients diagnosed with CRC develop distant metastases [1,2]. The lungs are the most common extra-abdominal site of metastases after curative resection of CRC [3]. In general, only 4.1% of patients with synchronous pulmonary metastases are treated with curative surgical intent [4]. However, the synchronous presence of lung metastases from CRC has been recognized as advanced metastatic disease, and few patients are candidates for surgery [5,6]. Mitry et al. [4] recently reported that the 3-year relative overall survival rate after pulmonary metastasectomy was 53.0% for synchronous metastases and 59.2% for metachronous metastases in a 30-year population-based study of 4,342 patients.

At our institution, the strategy for metastatic CRC has been to offer surgery rather than chemotherapy, as long as resectability and operability can be ensured. Even when surgical treatment is performed for both colorectal and pulmonary metastases, the sequence of surgical procedures has been dependent on the preferences of thoracic and colorectal surgeons. Since 2008, a single-stage approach was developed to perform synchronous lung metastasectomy in patients undergoing colorectal resection. This approach was safely performed in 22 patients with lung metastases. In this study, the single-stage approach reduced the length of hospital stay as compared to the 2-stage approach, even though the total operation time, estimated blood loss, postoperative morbidity, and total medical costs were similar in both groups. The reason for this is that the Korean healthcare system provides medical services, such as bed charges, at very inexpensive rates compared to other countries. However, minimally invasive surgery (VATS or laparoscopy) was performed more often in group S than in group T (Table 1), which indicated that the surgical strategy was dependent on the feasibility of minimally invasive surgery for thoracic or abdominal procedures.

The most important benefit of the single-stage approach is that it reduces additional hospital administration and anesthesia problems. Additional benefits are the avoidance of potential delays in surgical therapy for metastatic diseases and a lower risk of these metastases spreading if untreated. Moreover, additional factors, such as the risk of the interruption of chemotherapy, need to be considered when deciding whether to perform 2-stage or single-stage resections.

However, even though the benefits of the single-stage surgical strategy for synchronous pulmonary metastases are widely accepted, there is another question that remains unanswered. What is the sequence of pulmonary and colorectal resection? In other words, which should be performed first in a single-stage resection? This remains a controversial issue, but the complications of pulmonary metastasectomy are more significant; hence, these should be considered first when a longer-than-usual operation

time is expected.

Unfortunately, there is insufficient evidence to answer this question. Another reason why thoracic surgery should be considered first is that we can better understand the prognosis of patients who undergo single-stage resection because we cannot definitively determine whether the pulmonary nodule is a metastatic lesion until pathologically proven by surgical resection. Generally, pulmonary nodules are recognized as metastases on computed tomography scans, but they do not always represent true metastatic diseases. Inflammatory lesions or intrapulmonary lymph nodes can be mistaken for cancer in the lungs. In addition, for the detection of lung lesions, manual palpation is the most sensitive procedure to detect small lung lesions, which is one of the disadvantages of the single-stage approach because thoracic surgeons prefer to perform minimally invasive surgery due to the need for concomitant abdominal surgery. Some studies have reported that additional nodules detected by palpation did not affect long-term survival because of the high false-positive rate of small lung lesions [7,8]. However, a recent series demonstrated that manual palpation via open thoracotomy increased the number of pathologically confirmed malignant lesions compared to a thoracoscopic approach [9].

Indeed, the optimal management of patients with synchronous colorectal pulmonary metastases requires a multifactorial treatment strategy based on the symptoms, location, and extent of the disease, as well as the patient's performance status and underlying comorbidities. However, the crucial factors related to the selection of the surgical approach could not be demonstrated in this study. The validation and optimization of established treatment criteria and oncologic guidelines are imperative to further improve patient survival, morbidity, mortality, and length of hospital stay. Based on our experience, the proposed criteria for single-stage resection of CRC and pulmonary metastases should include the following: (1) relatively young patients (<65 years old), (2) no significant comorbidities, (3) peripheral pulmonary nodules, (4) oligometastases (<3–5 pulmonary metastases), (5) minimally invasive thoracic or abdominal surgery, and (6) no other sites of metastasis.

This study has several limitations, particularly the small size of the data set. Additionally, the patients were enrolled from a single institution, and the data were retrospectively reviewed. More evidence is needed to evaluate the proposed criteria for single-stage resection of CRC and pulmonary metastases. Until then, metastatic CRC is best treated with a team approach, including 1 or more surgeons, medical oncologists, and radiation oncologists, if needed. This practice will allow patients to have their cancer treated more quickly and efficiently in shorter hospital stays without increased risks.

In conclusion, by avoiding a second thoracic procedure, a single-stage approach for colorectal and pulmonary resection shortened the overall hospital stay with no changes in total medical costs, hospital mortality, and morbidity, despite the increased total operation time. Therefore, we suggest that a single-stage operation could be a good surgical strategy in selected patients.

Conflict of interest

No potential conflict of interest relevant to this article was reported.

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