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Surgical Intervention Improves Survival for Metastatic Non-Small Cell Lung Cancer Patients

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Abstract: Surgical intervention for stage IV non-small cell lung cancer (NSCLC) is still controversial. This study sought to evaluate the clinical effects of surgical intervention on survival in patients with stage IV NSCLCs and to identify the cohort benefitting the most from surgery.

A retrospective study from the Surveillance, Epidemiology, and End Results database was performed to compare the survival of stage IV NSCLC patients who had undergone surgery with those who did not undergo surgery. Overall survival (OS) was evaluated using the Kaplan–Meier method and the log-rank test. The Cox proportional hazards model was used for multivariate analysis.

The total number of eligible patients was 43,538, including 16.8% in the M1a stage and 83.2% in the M1b stage. The percentages of patients with no surgery (NONE), only metastatic tumor resection (MTR), only primary tumor resection (PTR), and both primary and metastatic tumor resection (PMTR) were 89.0%, 6.7%, 3.5%, and 0.8%, respectively; the corresponding 5-year survival rates were 2.0%, 4.0%, 13.0%, and 20.0%, respectively ($P < 0.001$); and the corresponding OS rates were 11.1 months, 14.7 months, 29.4 months, and 34.9 months, respectively ($P < 0.001$). Notably, the pairwise comparisons of 5-year survival rate and OS among the subgroups were all statistically significant. The multivariate analysis showed that surgical intervention was correlated with longer survival in patients with stage IV NSCLC. The stratified analysis showed significant differences in the OS on strata of the M1a stage and strata of the M1b stage. In the M1a stage, patients with PTR had significantly better OS than those with NONE ($P < 0.001$) or MTR ($P < 0.001$) but showed no significant differences compared with those with PMTR ($P = 0.174$); patients with MTR did not have prolonged survival compared with patients with NONE ($P = 0.185$), and they also did not have prolonged survival compared with patients with PMTR ($P = 0.052$). In the M1b stage, pairwise comparisons of OS were all statistically significant among the subgroups ($P < 0.001$).

Surgical intervention can prolong survival to different degrees according to the modalities of surgery in stage IV NSCLC.

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Abbreviations: 5YSR = 5-year survival rate, AJCC = American Joint Committee on Cancer, CEA = carcinoembryonie antigen, CI = confidence interval, HR = hazard ratio, KPS = Karnofsky performance score, MTR = only metastatic tumor resection, NONE = no surgery, NSCLC = non-small cell lung cancer, OS = overall survival, PMTR = both primary and metastatic tumor resection, PTR = only primary tumor resection, SAS = stereotactic radiosurgery, SEER = Surveillance, Epidemiology, and End Results, WBRT = whole-brain radiation therapy.

INTRODUCTION

Lung cancer is the leading cause of cancer-related deaths worldwide. The rate of overall survival (OS) of 5-year or more in all patients is only 16.6%.[1] Of all lung cancer patients, 57% are diagnosed with metastasis, and the 5-year relative survival rate (5YSR) of these patients is only 3.9%.[1] The most frequently metastatic site is the nervous system, followed by the bone, liver, lung, and adrenal gland.[2] Non-small cell lung cancer (NSCLC) is the major subgroup in the WHO classification of lung cancers, including more than 85% of all lung cancers.[1] Adenocarcinoma accounts for almost 50% of NSCLCs.[3] Almost all patients with metastatic disease are not eligible for curative treatments and do not have the option of surgery. According to the 2015 National Comprehensive Cancer Network NSCLC guidelines, of metastatic cases, surgical resection of a solitary brain metastasis is regarded as the only category 1 recommendation to expand survival, with a 5YSR of 10% to 20% and a median survival time of 40 weeks. However, other metastatic diseases, including solitary metastasis in other organs, remain controversial in terms of surgical intervention.[1] Solitary adrenal metastasis can be treated with local therapy for the adrenal lesion, such as adrenalectomy and radiotherapy, if the lung lesion is curable. However, it is only a category 2B recommendation. A solitary nodule in the contralateral lung with no lymph node metastasis (N0, M1a) can be considered to be two primary lung tumors if both are curable. Regarding other metastatic diseases, such as bone metastases, diffuse brain metastases, and disseminated metastases, systemic therapy, and palliative local therapy are the main choices.[1]

Despite a series of reports with small sample showed survival benefits among NSCLC patients with metastasis,[4–7] improved survival with surgical intervention has not been clearly defined. Additionally, the lack of randomized controlled trials makes it difficult to develop treatment guidelines for NSCLC patients with metastasis. Thus, we retrospectively analyzed the data of patients with stage IV NSCLC from the Surveillance, Epidemiology, and End Results (SEER) database to evaluate the

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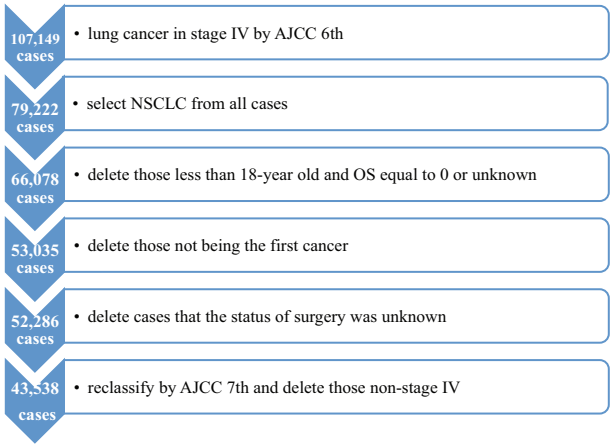

FIGURE 1. The procedures of selecting cases from SEER database from 2004 to 2007. AJCC: American Joint Committee on Cancer; NSCLC: non-small cell lung cancer; OS: overall survival; SEER: Surveillance, Epidemiology, and End Results.

survival benefits associated with surgical intervention and to identify the cohort benefitting the most from surgery.

MATERIALS AND METHODS

Data Sources and Patient Selection Criteria

The population for this retrospective cohort study was selected from the National Cancer Institute's SEER database, which is a cancer registry program that includes 26.2% of the population of the United States. To investigate the effects of surgical intervention on survival in stage IV NSCLC, lung cancers diagnosed as stage IV from January 1, 2004 to December 31, 2007 according to the criteria of the American Joint Committee on Cancer (AJCC) 6th edition were included in the study (Figure 1). Then, those cases were reclassified according to the criteria of the AJCC 7th edition. Exclusion criteria included: OS of less than 1 month (equal to 0) or unknown after confirmed diagnosis, age younger than 18 years, histology for small cell lung cancer or unknown, status of surgery unknown, and NSCLC not being the first cancer. Ultimately, 43,538 cases were included in our study. We obtained the permission to access the research data (Reference Number: 10904-Nov2014). Because our study used preexisting data with no personal identifiers, it was exempt from review by the Second Affiliated Hospital of Zhejiang University School of Medicine's review board.

Statistical Analysis

Patients included in the study were described according to year of diagnosis, age, sex, race, tumor location, grade, histology, TNM stage, and surgical intervention. In general, surgical intervention consisted of no surgery (NONE), only primary tumor resection (PTR), only metastatic tumor resection (MTR), and both primary and metastatic tumor resection (PMTR). OS analysis was performed using the Kaplan–Meier method. The log-rank test was performed to compare the differences in survival among those demographic and tumor factors, including year of diagnosis, age, sex, race, tumor location, grade, histology, TNM stage, and surgical intervention. The Cox proportional hazards model was also used to evaluate the effects of multiple variables on survival. A P value of <0.05 was considered statistically significant.

Statistical analysis was performed with the statistical software package SPSS version 19.0 (SPSS Inc., Chicago, IL). We used SEER*Stat, version 8.2.1.

RESULTS

Patient Characteristics

The total number of eligible patients was 43,538. Of these stage IV NSCLCs, patients were more likely to have had a tumor located in the upper lobe and to have been less than 75 years old, men, white, and diagnosed with adenocarcinoma (Table 1). Of the 43,538 patients, there were 16.8% (7321) in the M1a stage and 83.2% (36,200) in the M1b stage.

Regarding surgical intervention, the percentages of NONE, MTR, PTR, and PMTR were 89.0% (38,755), 6.7% (2923), 3.5% (1516), and 0.8% (344), respectively; the corresponding 5YSR were 2.0%, 4.0%, 13.0%, and 20.0%, respectively, which were statistically significant according to pairwise comparison; and the corresponding median survival times were 8.2 months, 9.3 months, 16.5 months, and 19.6 months, respectively. See Table 1 for other patient characteristics.

Correlation Between Surgical Intervention and Survival in Stage IV NSCLC

In the univariate analysis, statistically significant differences in OS were seen when patients were stratified by surgical intervention (Figure 2; Table 2). Based on the status of surgery, OS of NONE, MTR, PTR, and PMTR were 11.1 months (95% confidence interval [CI], 11.0–11.3 months), 14.7 months (13.9–15.5 months), 29.4 months (27.7–31.1 months) and 34.9 months (31.1–38.9 months), respectively, with a P value of <0.001. Notably, OS gradually increased with the changes of surgical approach, and pairwise comparisons for OS among the subgroups were all statistically significant. The corresponding 5YSR were 2.0%, 4.0%, 13.0%, and 20.0%, respectively ($P < 0.001$). Furthermore, the multivariate analysis was performed by using the Cox proportional hazards model, and surgical intervention was confirmed to correlate with survival in patients with stage IV NSCLC. Compared with patients with NONE, statistically better survival was shown with a hazard ratio (HR) of 0.836 (95% CI, 0.766–0.912; $P < 0.001$) for MTR, 0.523 (0.484–0.565; $P < 0.001$) for PTR, 0.340 (0.287–0.402; $P < 0.001$) for PMTR.

Considering the differences between M1a and M1b in AJCC staging, a stratified analysis based on the status of the M1 stage was performed by Kaplan–Meier analysis. The log-rank test indicated that there were significant differences in OS among the subgroups in both M1a and M1b stages. Pairwise comparisons of OS were all statistically significant among the subgroups of patients in the M1b stage ($P < 0.001$), whose OS was 10.0 months for NONE, 14.6 months for MTR, 24.7 months for PTR, and 35.2 months for PMTR (Figure 3, M1a and M1b; Table 3). Of those in the M1a stage, patients with PTR had significantly better OS (40.4 months, 95% CI, 36.9–43.8 months) than those with NONE (16.7 months, 16.2–17.3 months; $P < 0.001$) and MTR (18.9 months, 14.3–23.4 months; $P < 0.001$), whereas there was no significant difference in OS between patients with PTR compared with those with PMTR (28.2 months, 19.7–36.7 months; $P = 0.174$). However, patients in the M1a stage did not benefit from MTR compared with NONE ($P = 0.185$), or from MTR compared with PMTR

TABLE 1. Demographic and Tumor Information for Patients with Stage IV NSCLC

Variable	Number (%)
Year of diagnosis	
2004	10,739 (24.7%)
2005	10,669 (24.5%)
2006	11,117 (25.5%)
2007	11,013 (25.3%)
Age	
<75	31,844 (73.1%)
≥75	11,694 (26.9%)
Sex	
Male	24,139 (55.4%)
Female	19,399 (44.6%)
Race	
White	34,767 (80.0%)
Black	5479 (12.6%)
Other	3188 (7.3%)
Location	
Main bronchus	2086 (6.0%)
Upper lobe	20,631 (59.4%)
Middle lobe	1632 (4.7%)
Lower lobe	9864 (28.4%)
Overlapping lesions	522 (1.5%)
Grade	
Well	948 (2.2%)
Moderate	3812 (8.8%)
Poor	11,142 (25.6%)
Undifferentiated	1095 (2.5%)
Unknown	26,541 (61.0%)
Histology	
AC	18,509 (42.5%)
SC	6668 (15.3%)
LCC	1524 (3.5%)
NC	1263 (2.9%)
ASC	310 (0.7%)
SMC	233 (0.5%)
Other NSCLC	15,031 (34.5%)
T stage	
T1	5680 (16.7%)
T2	13,590 (40.0%)
T3	5009 (14.7%)
T4	9703 (28.6%)
N stage	
N0	9523 (25.5%)
N1	3211 (8.6%)
N2	18,246 (48.8%)
N3	6425 (17.2%)
M stage	
M1a	7321 (16.8%)
M1b	36,200 (83.2%)
Surgery	
NONE	38,755 (89.0%)
MTR	2923 (6.7%)
PTR	1516 (3.5%)
PMTR	344 (0.8%)

AC = adenocarcinoma, ASC = adenosquamous carcinoma, LCC = large cell carcinoma, MTR = only metastatic tumor resection, NC = neuroendocrine carcinoma, NONE = no surgery, NSCLC = non-small cell lung cancer, PMTR = both primary and metastatic tumor resection, PTR = only primary tumor resection, SC = squamous carcinoma, SMC = sarcomatoid carcinoma.

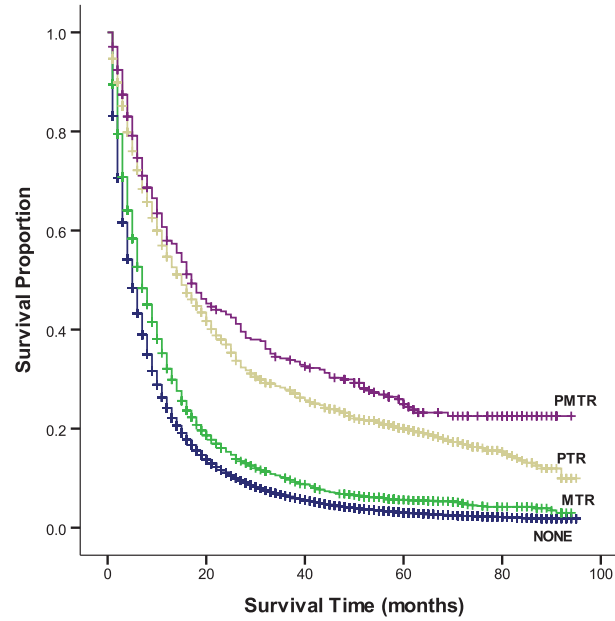

FIGURE 2. The Kaplan–Meier survival analysis based on the status of surgical management (no surgery [NONE], only metastatic surgery [MTR], only primary surgery [PTR], and both primary and metastatic surgery [PMTR]). The OS of each subgroup by pair-wise comparison was statistically significant ($P < 0.05$). OS: overall survival.

($P = 0.052$), and those patients had worse OS compared with PTR ($P < 0.001$).

The Prognostic Factors for Surgical Intervention

In addition, we analyzed prognostic factors in patients who had undergone surgery in stage IV, to identify the cohort benefitting the most from surgery. In our analysis above, we selected again to obtain a new cohort of 4783 cases who had undergone at least one kind of surgery. In the univariate analysis using the Kaplan–Meier method, among these stage IV NSCLC patients who had undergone surgery, the year of diagnosis, age,

TABLE 2. The Association Between Surgical Resection and Overall Survival by Kaplan–Meier Method in Stage IV NSCLC

	Number (%)	OS (Months)	95% CI (Months)	*P*
Surgery				<0.001*
NONE	38,755 (89.0%)	11.1	11.0–11.3	
MTR	2923 (6.7%)	14.7	13.9–15.5	
PTR	1516 (3.5%)	29.4	27.7–31.1	
PMTR	344 (0.8%)	34.9	31.1–38.9	

CI = confidence interval, MTR = only metastatic tumor resection, NONE = no surgery, NSCLC = non-small cell lung cancer, OS = overall survival, PMTR = both primary and metastatic tumor resection, PTR = only primary tumor resection.

*Statistically significant prognostic factor identified by univariate/multivariate analysis.

TABLE 3. The Influence of the Status of M1 on Selecting Surgical Management by Kaplan–Meier Method in Stage IV NSCLC

	OS (Months)	95% CI (Months)	*P*
M1a			<0.001*,†
NONE	16.7	16.2–17.3	
MTR	18.9‖	14.3–23.4	
PTR	40.4§	36.9–43.8	
PMTR	28.2	19.7–36.7	
M1b			<0.001*,†,‡
NONE	10.0	9.8–10.1	
MTR	14.6	13.8–15.4	
PTR	24.7	22.9–26.5	
PMTR	35.2	31.1–39.3	

CI = confidence interval, MTR = only metastatic tumor resection, NONE = no surgery, NSCLC = non-small cell lung cancer, OS = overall survival, PMTR = both primary and metastatic tumor resection, PTR = only primary tumor resection.

*Statistically significant prognostic factor identified by univariate/multivariate analysis.

†The *P* value of log-rank test on each substratification.

‡The *P* value of log-rank test among pairwise comparisons.

§Patients with PTR in M1a stage had significant better OS compared with those with NONE ($P < 0.001$) or MTR ($P < 0.001$), but had no significant difference compared with those with PMTR ($P = 0.174$).

‖Patients with MTR cannot prolong survival compared with patients with NONE ($P = 0.185$) and they also cannot prolong survival compared with patients with PMTR ($P = 0.052$), but they had a worse OS compared with PTR ($P < 0.001$).

sex, race, tumor location, grade, histology, TNM stage, and undergoing surgery were all significantly associated with OS (Table 4). In the multivariate analysis with the Cox proportional hazards model, being less than 75 years old, women, non-white and non-black, as well as having well differentiated, low T stage, low N stage, M1a stage, PTR, and PMTR were favorable prognostic factors for survival in patients with stage IV NSCLC who had undergone surgery (Table 4).

DISCUSSION

The aim of this retrospective cohort study was to investigate the necessity of surgical intervention for stage IV NSCLC patients. In our study, 43,538 patients were included, and 4783 of them had undergone surgery including PTR, MTR, and PMTR, which represented 11.0% of the total cohort. In our cohort, the 5YSR were 2.0% for NONE, 4.0% for MTR, 13.0% for PTR, and 20.0% for PMTR, and the pairwise comparisons among the subgroups were all statistically significant. The corresponding OS were 11.1 months for NONE, 14.7 months for MTR, 29.4 months for PTR, and 34.9 months for PMTR. Moreover, the 5YSR of PTR and PMTR were apparently superior to the published rate of 3.9% for stage IV lung cancer.[1] Then, a stratified analysis in terms of M1a and M1b stages was performed. Compared with NONE, PTR and PMTR were associated with better survival in both the M1a and M1b stages, but MTR was associated with better survival only in the M1b stage. The failure to benefit from MTR may be attributable to unresectable metastatic tumors in the M1a stage, which included separate tumor nodule(s) in a contralateral lobe, tumors with pleural nodules, and malignant pleural (or pericardial) effusion.[1] The results indicated that patients in the M1a stage could only benefit from PTR ($P < 0.001$), and MTR may not be necessary, whereas patients in the M1b stage may benefit from aggressive treatment including MTR, PTR, or PMTR, if the tumor is resectable.

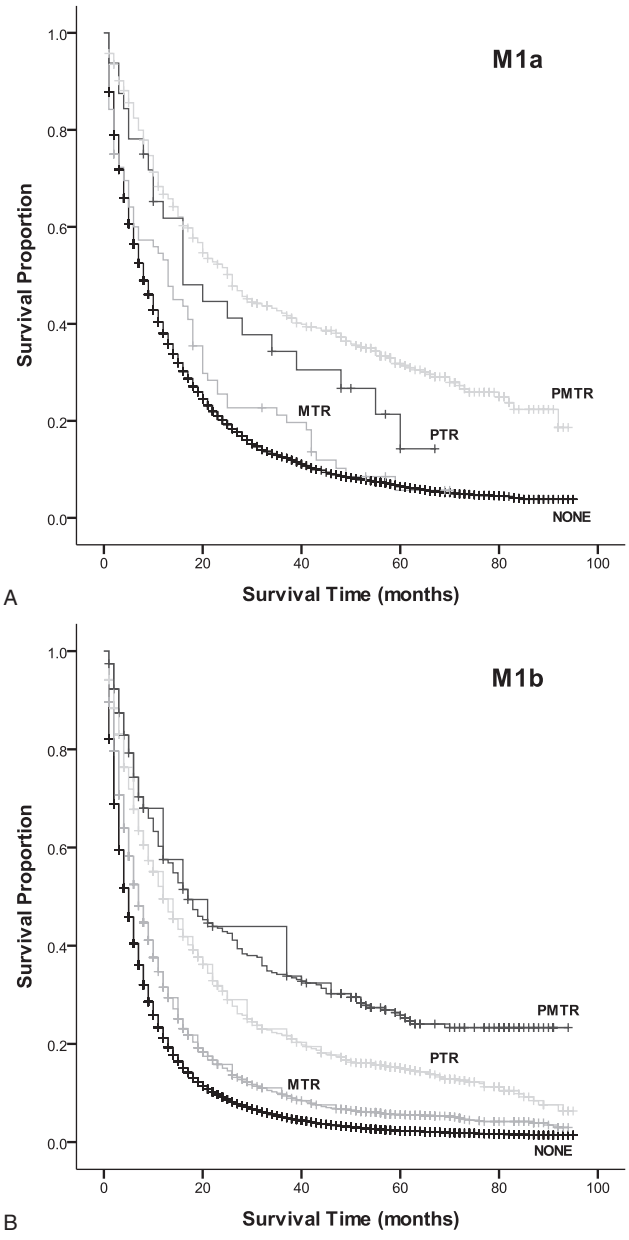

FIGURE 3. In the stratified analysis between M1a and M1b, the Kaplan–Meier survival analysis based on the status of surgical management (no surgery [NONE], only metastatic surgery [MTR], only primary surgery [PTR], and both surgery [PMTR]). The *P* value of each substratification by log-rank test was statistically significant ($P < 0.05$).

Regardless of differences in metastatic sites, prolonged survival of stage IV NSCLC patients who had undergone surgery for primary and metastatic tumors has also been reported in several studies.[8,9] Hanagiri et al[9] have conducted

TABLE 4. Prognostic Factors for OS in Stage IV NSCLC with Surgery by Univariate and Multivariate Analyses

	Univariate Analysis			Multivariate Analysis		
Variable	**OS (Months)**	**95% CI (Months)**	***P***	**HR**	**95% CI**	***P***
Year of diagnosis			0.041*			
2004	20.2	18.6–21.7				
2005	18.7	17.4–20.1				
2006	19.1	17.8–20.4				
2007	18.8	17.6–19.9				
Age			<0.001*			
<75	21.5	20.6–22.3		1		
≥75	17.6	15.6–19.6		1.406	1.213–1.629	<0.001*
Sex			<0.001*			
Male	18.5	17.5–19.5		1		
Female	23.6	22.3–24.9		0.857	0.770–0.954	0.005*
Race			0.002*			
White	20.7	19.8–21.5		1		
Black	19.8	17.5–22.0		1.136	0.970–1.331	0.114
Other	25.7	22.4–29.0		0.753	0.595–0.952	0.018*
Location			<0.001*			
Main bronchus	15.1	11.6–18.7				
Upper lobe	22.1	21.0–23.3				
Middle lobe	25.8	21.3–30.3				
Lower lobe	20.3	18.7–22.0				
Overlapping lesion	20.3	14.5–26.1				
Grade†			<0.001*			
Well	43.0	37.3–48.7		1		
Moderate	29.4	26.6–32.2		1.314	1.026–1.682	0.030*
Poor	21.2	19.7–22.7		1.409	1.187–1.906	0.001*
Undifferentiated	16.7	12.9–20.4		1.720	1.354–2.470	<0.001*
Histology			<0.001*			
AC	22.4	21.3–23.6				
SC	19.6	17.5–21.8				
LCC	17.3	13.4–21.3				
NC	35.1	30.2–40.0				
ASC	17.4	12.1–22.7				
SMC	13.7	6.5–21.0				
Other NSCLC	16.4	15.0–17.8				
T stage	<0.001*					
T1	26.0	23.9–28.1		1		
T2	20.9	19.6–22.2		1.223	1.057–1.417	0.007*
T3	19.1	16.7–21.6		1.576	1.308–1.899	<0.001*
T4	19.5	17.9–21.2		1.321	1.119–1.560	0.001*
N stage			<0.001*			
N0	26.9	25.2–28.6		1		
N1	22.4	19.8–25.0		1.249	1.059–1.473	0.008*
N2	16.3	15.2–17.3		1.346	1.187–1.526	<0.001*
N3	13.3	11.6–15.0		2.153	1.754–2.642	<0.001*
M stage			<0.001*			
M1a	37.1	34.1–40.1		1		
M1b	18.7	17.9–19.5		1.557	1.322–1.834	<0.001*
Surgery†			<0.001*			
MTR	14.7	13.9–15.5		1		
PTR	29.4	27.7–31.1		0.631	0.557–0.715	<0.001*
PMTR	34.9	31.1–38.8		0.421	0.346–0.512	<0.001*

AC = adenocarcinoma, ASC = adenosquamous carcinoma, CI = confidence interval, HR = hazard ratio, LCC = large cell carcinoma, MTR = only metastatic tumor resection, NC = neuroendocrine carcinoma, NONE = no surgery, NSCLC = non-small cell lung cancer, OS = overall survival, PMTR = both primary and metastatic tumor resection, PTR = only primary tumor resection, SC = squamous carcinoma, SMC = sarcomatoid carcinoma.

*Statistically significant prognostic factor identified by univariate/multivariate analysis.

†The log-rank test of OS among subgroups by pairwise were all statistically significant.

a retrospective study in 36 Japanese patients who had undergone PTR and local therapy for NSCLC with oligometastatic disease. The local therapy for metastatic disease included radiation for bone metastasis, stereotactic radiosurgery (SAS) for brain metastasis, and surgical resection for adrenal, axillary lymph node, and contralateral lung metastasis. The postoperative 5YSR of all of the patients, patients with pleural metastasis (M1a stage), and patients with distant metastasis (mainly M1b stage and one with contralateral lung metastasis) were 26.8%, 25.3%, and 30.1%, respectively. Unfortunately, they did not perform comparisons of survival among the three subgroups. In another Japanese investigation, the overall 5YSR of stage IV NSCLC patients was only 5.8%, whereas the 5YSR was 41.0% in stage IV NSCLC patients with surgery.[10] Goya et al[11] have shown a 20.0% survival rate at 5 years in patients with stage IV NSCLC who had undergone PTR. Although there was a lack of comparisons between the surgical and non-surgical groups in the three studies mentioned above, an apparent improvement in 5YSR has been reported for stage IV NSCLCs with surgery compared with the published 5YSR of 3.9% in all stage IV NSCLCs. Therefore, surgical intervention may be a choice for extending the survival time of stage IV NSCLC patients.

In addition, most published studies have been designed under the condition of a single metastatic type. A randomized trial has been designed to evaluate the efficacy of neurosurgery plus whole-brain radiation therapy (WBRT) vs. stereotactic radiosurgery (SRS) plus WBRT in NSCLC patients with single brain metastases. The former modality prolonged survival, but no significant survival difference was observed compared with the latter one.[12] In other words, surgical intervention can prolong OS in patients with single brain metastasis. Subsequently, the equal efficacy was validated by several studies.[13–15] To date, the two modalities are recommended for NSCLC patients with solitary brain metastasis as standard therapies.[1] Regarding solitary adrenal metastasis, the survival benefit from adrenalectomy has been determined in patients with metastatic lung cancer at the Mayo Clinic in Rochester when compared with those without MTR from the SEER database ($P = 0.002$) whose median OS was 3.5 and 1.1 years, respectively.[16] To date, local therapy for adrenal metastasis from NSCLC has become a therapeutic option if the lung lesion is curable, which is considered evidence of category 2B.[1]

However, controversial conclusions regarding survival benefits from surgical intervention for stage IV NSCLC have also been reported. Kim et al[17] have divided 22 NSCLC patients with synchronous brain metastases who all presented with neurological symptoms but without PTR into two groups (the neurosurgery group and the non-neurosurgery group). They have demonstrated that neurosurgery has no survival benefit ($P = 0.550$) but alleviates the neurological symptoms ($P = 0.0495$) compared with the non-neurosurgery group, with OS in the neurosurgery group, and the non-neurosurgery group of 12.1 months and 10.2 months, respectively. Le Pimpec Barthes et al[18] have performed a study in stage IV NSCLC patients undergoing lung resection, dividing the patients into two groups (PTR and PMTR) according to the status of metastatic surgery. In the M1b stage, PMTR had no significant survival benefit compared with PTR ($P = 0.67$), and the 5YSRs were16.7% and 15.6%, respectively, results different from those in our study. Okubo et al[19] have demonstrated that only simultaneous same lobe metastasis of NSCLC, rather than other metastatic types in M1a stage, can benefit from surgery.

To analyze the characteristics of patients receiving surgery, we performed univariate and multivariate analyses in stage IV NSCLC patients who had undergone surgery. Being less than 75 years old, women, non-white and non-black, as well as having well differentiated, low T stage, low N stage, M1a stage, PTR, and PMTR were favorable prognostic factors. Therefore, we propose that patients who were less than 75 years old, women, and had low T and N stage are suitable for surgery. In the M1a stage, patients should undergo only PTR. In the M1b stage, patients can choose among MTR, PTR, or PMTR, if they can be tolerated. Moreover, Modi et al[20] have noted that the absence of mediastinal lymph nodes is a favorable prognostic factor for PMTR in stage IV NSCLC patients. Adenocarcinoma, low carcinoembryonie antigen (CEA) levels at presentation, response to preoperative chemotherapy before local treatment and a high Karnofsky performance score are indicators of better survival.

There are some limitations in the current study. The main limitation is that it was a retrospective study, and therefore some important information could not be acquired, such as metastatic site, number of metastatic tumors, treatment before and after surgery, length of course, resection type (complete or incomplete), and the sequence of PMTR (synchronous or metachronous). Riihimaki et al[2] have revealed that patients with liver (HR 1.53) and bone (1.16) metastases had worse survival compared with patients with nervous system metastases, which had comparable survival to those with lung and adrenal metastases. Endo et al[21] have performed a prospective study in clinical T1–2N0–1 lung cancer patients with oligometastasis. Of 34 eligible patients, 20 of them had undergone complete resection of PMTR with a 5YSR of 44.7%, whereas the 10 patients undergoing incomplete resection of PTR had a 5YSR of 20%. This result indicates that complete resection results in better survival than incomplete resection. Additionally, because the proportion of patients undergoing surgery was only 11.0% (4783 cases) in the current study, the results may appear biased to some extent. Large sample sizes and, in particular, randomized controlled trials are needed to validate the effects of surgery on the survival of stage IV NSCLC patients.

CONCLUSIONS

Surgical intervention can prolong survival to different degrees according to the modalities of surgery in stage IV NSCLC patients. Considering the differences in metastatic sites, suitable patients should be selected before undergoing surgery. Patients in M1a stage should undergo only PTR, and MTR may not be necessary, whereas patients in M1b stage may benefit from aggressive treatment including MTR, PTR, or PMTR.

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