The surgical management of early-stage lung adenocarcinoma: is wedge resection effective?

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Background: The aim of the study was to explore the outcomes of wedge resection on patients with early-stage lung adenocarcinoma (LUAD) and further identify potential prognostic factors for these patients.

Methods: A retrospective cohort of 190 patients (99 solitary LUAD and 91 multifocal LUAD) undergone wedge resection from October 2014 to September 2015 was established. Cox proportional-hazards model was used to evaluate the significant clinical prognostic factors. Further, data on patients with multifocal adenocarcinoma after segmentectomy were retrieved and propensity score matching was used to compare the outcomes of patients with multiple pulmonary nodules (MPNs) after wedge resection and segmentectomy.

Results: The 5-year overall survival (OS), progression-free survival (PFS), and lung cancer specific survival of the 190 patients after wedge resection were 95.5%, 87.9%, and 97.7%, respectively. Multivariable analysis showed that MPN [hazard ratio (HR) 3.07; 95% confidence interval (CI), 1.05–8.98] and solid-dominant lesions (HR 15.87; 95% CI, 2.38–105.84) were independently associated with worse PFS. Further, propensity score matching analysis showed that MPN patients had better PFS after segmentectomy compared with wedge resection (94% *vs.* 80.9%, P=0.008). MPN patients were more likely to perform systematic mediastinal nodal sampling (95.6% *vs.* 59.3%, P<0.001) after segmentectomy compared to patients who underwent wedge resection.

Conclusions: Wedge resection is a practical option for appropriately selected early-stage LUAD where tumor size is less than 2 cm and has a consolidation-to-tumor ratio ≤0.5. However, for MPNs, wedge resection may be not reliable and alternative procedures such as segmentectomy should be used.

Keywords: Wedge resection; segmentectomy; early-stage lung cancer; surgical oncology

Introduction

Lung cancer is the leading cause of cancer-related death worldwide, with non-small cell lung cancer (NSCLC) accounting for about 85% of the incident cases, causing a five-year survival rate of 19% (1,2). At present, an increasing number of early-stage lung cancer can be detected using thin-section computed tomography (TSCT).

Although, the current gold standard surgical procedure for NSCLC is still lobectomy (3,4), sublobar resection (SLR) which includes wedge resection and segmentectomy have been reported to be effective by GGOs (ground-glass opacities) (5-8). Further, SLR is recommended for early-stage NSCLC patients with low tolerance for lobectomy (9-11).
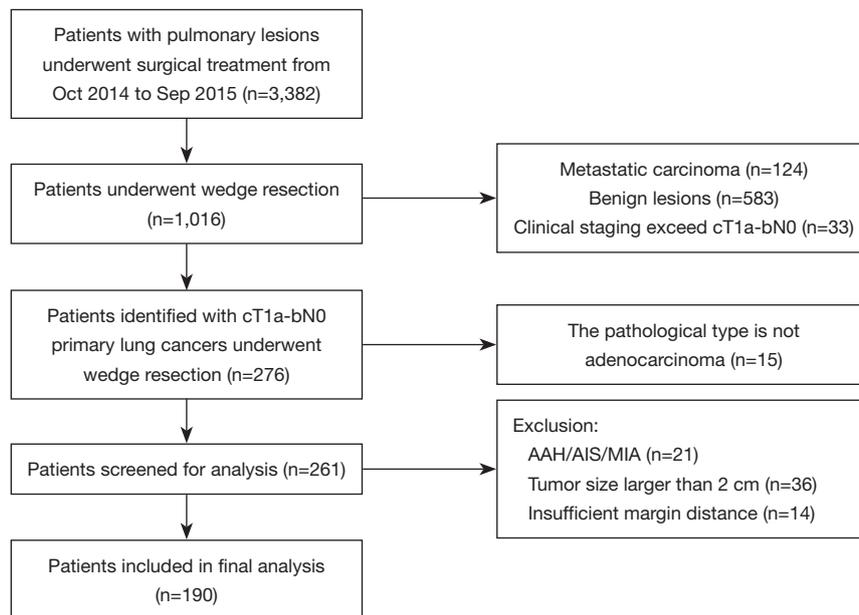
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Figure 1 The flow diagram of the patient selection. AAH, atypical adenomatous hyperplasia; AIS, adenocarcinoma in situ; MIA, microinvasive adenocarcinoma.

Although, several studies have compared survival outcome of wedge resection and segmentectomy (12-16), it is not clear which procedure is more reliable for peripheral lung nodules. Most studies have reported similar prognosis for segmentectomy and wedge resection on patients with stage IA NSCLC less than 1.0 cm (17,18), but the outcomes were unclear for 1.0–2.0 cm tumors with different consolidation-to-tumor ratio (CTR) (19-21). Besides, an international consensus has not been reached for an effective surgery procedure for synchronous multifocal nodules proven or suspected to be multiple primary lung cancer. Although a meta-analysis published in 2019 recommended that SLR is effective for multifocal nodules (22), the wedge resection outcomes of patients with multiple pulmonary nodules (MPNs) remain unclear and few studies have reported comparison of MPN prognosis and solitary pulmonary nodule (SPN).

It is widely accepted that "margin distance (MD)" is a crucial factor affecting the prognosis of wedge resection (23-25). In this study, we aimed at exploring the outcomes of wedge resection with sufficient MD (MD ≥20 mm or larger than tumor size) and identify prognostic factors of patients with early lung adenocarcinoma (LUAD) after undergoing wedge resection. Further, outcomes of patients with MPN who underwent wedge resection or segmentectomy were

evaluated.

We present the following article in accordance with the STROBE reporting checklist (available at http://dx.doi.org/10.21037/jtd-20-3005).

Methods

Patients selection

This is a single-center retrospective study of the outcomes of early-stage adenocarcinoma patients after wedge resection. We prospectively collected patient data and retrospectively observed the patients. Data between October 2014 and September 2015 were retrieved from the Department of Thoracic Surgery, National Cancer Center database. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). This study was approved by ethics committee of National Cancer Center/ Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College (approval number: 191137-1921). The requirement of patients' informed consent was waived owing to the retrospective nature of the study.

Inclusion criteria were as follows (*Figure 1*): (I) surgical approach was wedge resection; (II) clinical stage was T1a-bN0; (III) the pathological type was primary adenocarcinoma (for multifocal NSCLC, each resected

lesion was pathologically confirmed as independent adenocarcinoma). Exclusion criteria were: (I) the pathological type is atypical adenomatous hyperplasia (AAH), adenocarcinoma *in situ* (AIS) or minimally adenocarcinoma (MIA); (II) tumor size is larger than 2 cm; (III) insufficient margin distance: including positive surgical margin, MD <20 mm or less than a maximum diameter of the tumor; (IV) patients with previous treatment for lung cancer.

Radiological evaluation

In solitary pulmonary nodule (SPN), tumor size was defined as the maximum diameter of the lesion on CT scan. In MPNs, tumor size was defined as the maximum diameter of the main focus on CT scan. Main focus was defined as the main lung cancer to be surgically resected from its tumor size and radiological invasiveness. The comparison of clinicopathologic characteristics between SPN and MPN patients in this cohort is shown in Table S1. We examined consolidation tumor ratio (CTR) from the lung window of thin-section CT. Radiological criteria of CTR 0.5 as a cut-off was used in this study and cases were classified into two subgroups: GGO-dominant (CTR ≤0.5) and solid-dominant (CTR >0.5) based on previous studies (26,27).

Surgical procedure

Surgeries selected in this study were performed using thoracoscopic approach (single-port or three-port) without conversion to thoracotomy. Wedge resection or segmentectomy were performed to remove the main foci as well as secondary lesions on the same side. The indications for these patients underwent wedge resection are shown in Figure S1. And anatomic segmentectomy was performed for the segmentectomy group for main focus of MPN. Tumor characteristics and surgeon preference inform which sublobar procedure to perform (i.e., wedge resection or segmentectomy).

For wedge resection, we use preoperative CT-guided coil or intraoperative finger palpation to localize nodules. For segmentectomy, Three-dimensional reconstruction was used to ascertain the location of the nodules and the appropriate target segment. A systematic mediastinal nodal sampling was performed in all solid-dominant cases. Lymph node sampling was optional for GGO-dominant lesions.

Pathologic diagnosis and postoperative follow-up

Pathological sections used in this study were reviewed by

an experienced senior pathologist. Pathologic diagnosis was based on the 2015 World Health Organization (WHO) classification of lung cancer. Staging standard was based on the 8th edition of the Union for International Cancer Control/American Joint Committee on Cancer (UICC/AJCC) TNM staging for NSCLC (28,29). Cases with MPN were clinically and pathologically diagnosed as multiple primary lung cancer according to the 8th edition of the International Staging System of Lung Cancer as proposed by the AJCC (30). The degree of tumor histological differentiation was divided into three grades: I, well-differentiated; II, moderately differentiated; III, poorly differentiated.

Follow-up data on all patients were obtained from latest medical records or imaging examinations. Out-patient review was conducted every 3 months for the first 2 years, every 6 months for the subsequent 2 years, and annually thereafter for a lifetime. Overall survival (OS) was calculated from surgery to death irrespective of cause of death. Lung cancer-specific survival (LCSS) was calculated from surgery to death due to lung cancer. Progression-free survival (PFS) was recorded as number of months from surgery to the time recurrence or metastasis was first confirmed by assessment of imaging examination. Censoring was calculated as the patients who were still alive or "lost to follow-up."

Statistical analysis

Pearson Chi-square test or Fisher's exact test was used to compare categorical variables. Mann-Whitney U test was used to compare continuous variables using SPSS 18.0 software (IBM Corporation, Armonk, NY, USA). Continuous variables were presented as median (interquartile range). Survival curves of 5-year OS, PFS, and LCSS were generated using Kaplan-Meier method and statistically analyzed using the log-rank test. Univariate and multivariate analyses using Cox proportional-hazards models were carried out to identify significant clinical predictors of outcome using R 3.6.2 (https://www.r-project.org/).

For further comparison of the effect of resection type on synchronous multifocal nodules, patients undergoing segmentectomy were extracted from our database as controls. A flow diagram of patient selection process is provided separately (see Figure S2). Propensity score matching (PSM) method was used to eliminate selection biases. In this study, the propensity score was calculated based on preoperative factors such as sex, age, tumor size (based on main focus), preoperative CT features (based on

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Table 1 Patients' clinicopathologic characteristics of wedge resection

Clinicopathologic characteristic	Value
Age, y (range)	61 [52–69]
BMI, (range)	23.9 (22.1–26.3)
Tumor size, cm (range)	1.3 (0.9–1.5)
Gender, n (%)	
Female	124 (65.3)
Male	66 (34.7)
Smoking history, n (%)	
Ever	48 (25.3)
Never	142 (74.7)
Family history of carcinoma, n (%)	
Yes	68 (53.0)
No	122 (49.0)
Clinical T stage, n (%)	
cT1a	141 (74.2)
cT1b	49 (25.7)
If multiple, n (%)	
Yes	91 (47.9)
No	99 (52.1)
Imaging feature, n (%)	
GGO-dominant	133 (70.0)
Solid-dominant	57 (30.0)
Pathologic T stage, n (%)	
pT1a	84 (44.2)
pT1b	58 (30.5)
pT2a [Vis PI]	48 (25.3)
Number of cases with systematic mediastinal nodal sampling, n (%)	104 (54.7)
LN sampling number, n (range)	3.5 (0–7)
Pathologic N stage, n (%)	
N0/Nx	188 (98.9)
N1/2	2 (1.1)
Histological differentiation, n (%)	
Grade I	116 (61.1)
Grade II	54 (28.4)
Grade III	20 (10.5)

Table 1 (*continued*)

Table 1 (*continued*)

Clinicopathologic characteristic	Value
Vis PI, n (%)	
Yes	48 (25.3)
No	142 (74.7)
MVI, n (%)	
Yes	7 (3.7)
No	183 (96.3)
Pathological subtype, n (%)	
Lepidic/Acinar	125 (65.8)
Papillary	47 (24.7)
Micropapillary	9 (4.7)
Mucinous adenocarcinoma	9 (4.7)

BMI, body mass index; MPN, multiple pulmonary nodules; MVI, microscopic vascular invasion; OS, overall survival; PFS, progression-free survival; Vis PI, visceral pleura invasion.

main focus), and clinical T stage, which may influence the choice for surgical modes. Patients in the wedge resection group and segmentectomy group were matched in a 1:1 ratio according to their propensity scores. P<0.05 was considered statistically significant.

Results

Clinicopathologic characteristics and oncology outcomes

In this study, all 190 patients with LUAD who underwent wedge resection had a median postoperative follow-up period of 51 months (interquartile range 45.5–59 months). Clinicopathologic characteristics of patients are summarized in *Table 1*. In this study, the cut-off value of tumor size was set at 1.2 cm whereas sensitivity and specificity of PFS were 85% and 52.4%, respectively.

The cumulative 5-year OS, PFS and LCSS were 95.5%, 87.9%, and 97.7%, respectively. A total of eight patients died during the follow-up period. Out of the eight deaths, four were lung cancer-specific deaths whereas the other four from were due to other causes (cardiovascular or cerebrovascular accidents and postoperative respiratory failure). Twenty patients showed tumor progression during follow-up. Details on the 20 patients are shown in Table S2.

Table 2 Univariate and multivariate analysis of PFS after wedge resection

Variables	Univariate analysis			Multivariate analysis		
	HR	P value	95% CI	HR	P value	95% CI
Gender (reference: female)	2	0.13	0.82, 4.7			
Age	1	0.59	0.97, 1.1			
Smoking history (reference: never)	2.1	0.09	0.88, 5.3			
Tumor history (reference: no)	0.86	0.75	0.34, 2.2			
BMI	0.93	0.31	0.82, 1.1			
Vis PI (reference: no)	3.8	<0.01	1.6, 9.1	1.5	0.42	0.56, 4.02
MVI (reference: no)	5	0.01	1.4, 17	0.57	0.45	0.14, 2.41
If multiple (reference: SPN)						
MPN	3.8	0.01	3.8, 10	3.07	0.04	1.05, 8.98
Tumor size (reference: ≤1.2 cm)						
>1.2 cm	3	0.03	1.1, 7.7	2.06	0.16	0.76, 5.61
Histological differentiation (reference: grade I)						
Grade II	6	<0.01	1.86, 25.41	0.9	0.91	0.16, 4.98
Grade III	18	<0.01	4.94, 70.4	1.9	0.48	0.31, 11.74
Imaging features (reference: GGO-dominant)						
Solid-dominant	26	<0.01	5.9, 110	15.87	0.004	2.38, 105.84
Pathological subtype (reference: lepidic/acinar)						
Papillary	1.47	0.46	0.53, 4.05			
Micropapillary	3.03	0.15	0.66, 13.84			
Mucinous adenocarcinoma	2.58	0.22	0.57, 11.8			

BMI, body mass index; HR, hazard ratio; MPN, multiple primary nodules; MVI, microscopic vascular invasion; SPN, solitary pulmonary nodule; Vis PI, visceral pleura invasion.

Independent prognostic factors of patients

Cox proportional hazards model was used to analyze independent prognostic factors of PFS. Analysis of OS and LCSS was not included due to good outcomes of this well-selected cohort. This oncological outcome showed that wedge resection has a satisfactory 5-year survival for appropriately selected patients with early-stage LUAD.

Results from univariate analysis showed that MPNs, visceral pleura invasion (Vis PI), microscopic vascular invasion (MVI), tumor size (>1.2 cm), histological differentiation, and imaging features (solid-dominant) had significant effects on PFS (*Table 2*). Notably, MPN (*vs.* SPN) were associated with poor PFS (80.9% *vs.* 94.1%, P<0.01). Parameters obtained from histopathology,

including Vis PI (P=0.003) and MVI (P=0.01), were significant, however pathological subtype (all P>0.05) was not significant. Analysis on factors associated with imaging features, showed that patients with GGO-dominant lesions had superior PFS compared with patients with solid-dominant lesions (98.3% *vs.* 63.5%, P<0.01). Moreover, analysis of tumor histological differentiation showed that moderately differentiated (P<0.01) and poorly differentiated (P<0.01) adenocarcinoma had lower PFS compared with well-differentiated adenocarcinoma. Tumor size larger than 1.2cm had significant effect on PFS (P=0.03).

Multivariable analysis results based on the Cox model are shown in *Table 2*. MPN [hazard ratio (HR) 3.07; 95% confidence interval (95% CI), 1.05–8.98; P=0.04] and solid-dominant lesions (HR 15.87; 95% CI, 2.38–105.84;
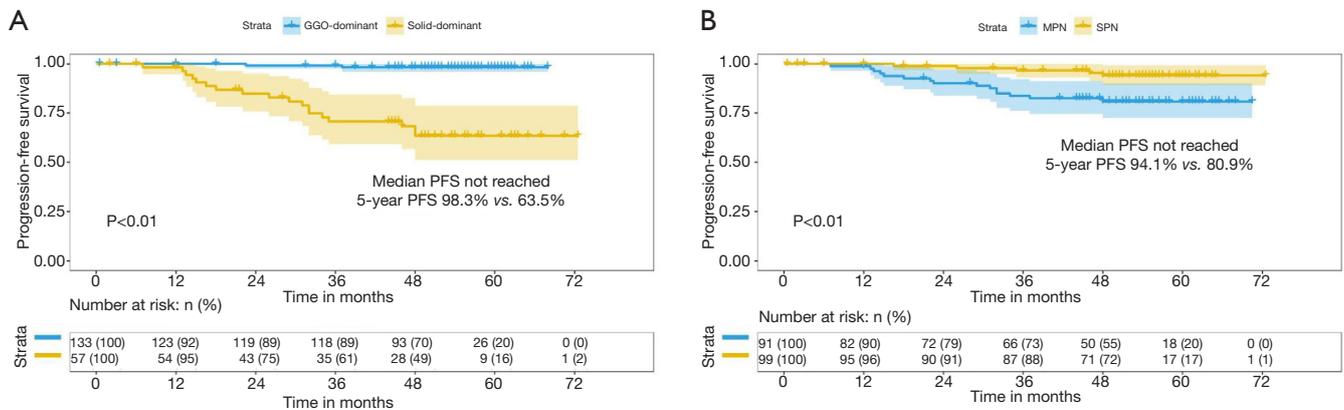
Figure 2 Progression-free survival of 190 patients underwent wedge resection. (A) Patients in GGO-dominant group had superior PFS compared with patients in solid-dominant group (98.3% *vs.* 63.5%, P<0.01). (B) Patients in MPN group had worse PFS compared with patients in SPN group (80.9% *vs.* 94.1%, P<0.01). MPN, multiple pulmonary nodule; SPN, solitary pulmonary nodules; PFS, progression-free survival.

P=0.004) were the only independent prognostic factors associated with poor PFS (*Figure 2*).

Analysis of propensity-matched groups

To further understand the effect of surgical type on PFS in patients with MPN, a series of patients who had undergone segmentectomy were selected from our database (see Figure S2). Baseline Characteristics of MPN before propensity score matching is showed in Table S3. We hypothesized that wedge resection and segmentectomy are associated with comparable oncologic outcomes for patients with multiple primary lung cancer. A propensity-matched analysis was performed between wedge resection group (91 cases) and segmentectomy group (125 cases). After matching, clinicopathologic characteristics of the matched patients (91 cases in each group) were evaluated as shown in *Table 3*.

Patients with MPN undergoing segmentectomy were more likely to perform systematic mediastinal nodal sampling (95.6% *vs.* 59.3%, P<0.001) and had more totally LNs sampled compared with wedge resection group (10 *vs.* 4, P<0.001). Therefore, patients in wedge resection group had a marginally lower frequency of pN1/N2 compared with segmentectomy group (1.1% *vs.* 6.6%, P=0.054). At a median follow-up of 51 months, tumor progression was noted in five patients undergoing segmentectomy and fifteen patients undergoing wedge resection. Patients with MPN in segmentectomy group had better PFS than wedge resection group (94% *vs.* 80.9%, P=0.008) (*Figure 3*).

Discussion

In this retrospective study, patients with early-stage adenocarcinoma who were well-selected could have an excellent 5-year OS and PFS after wedge resection. CTR >0.5 and MPNs were identified as two independent factors for PFS for wedge resection cohort. Therefore, wedge resection may be more suitable to patients with solitary nodules ≤2 cm with a CTR ≤0.5. In addition, the 5-year PFS of segmentectomy group were significantly higher than wedge resection group in patients with MPN. These findings imply that precise preoperative planning should be done before carrying out resections of MPNs.

Several studies on prognosis after wedge resection in patients with early stage lung cancer have been carried out. The outcomes of 5-year OS and LCSS in our study were comparable to or better than most previous studies (14,20,21,31). In 2017, JCOG0804 study reported its primary endpoint that sublobar resection, mainly wedge resection, offered sufficient local control and RFS (99.7%) for peripheral NSCLC (≤2 cm, CTR ≤0.25) on TSCT. In this study, GGO-dominant SPN results (≤2 cm, CTR ≤0.5, 5-year RFS 98.3%) agreed with JCOG0804 survival outcomes results. However, findings from previous studies on wedge resection only apply to cohorts of patients with solitary nodule. Patients in our cohort were consciously selected for wedge resection, and it may be clinically significant given the increase in the proportion of multifocal nodules.

Table 3 Characteristics of propensity-matched groups

Variables	Wedge resection	Segmentectomy	P value
Age, y (range)	61 (53–66.5)	60 (54–66)	0.724
Female sex, n (%)	60 (65.9)	66 (72.5)	0.335
Tumor size, cm (range)	1.3 (1.05–1.6)	1.4 (1.1–1.8)	0.09
Clinical T stage, n (%)			0.746
cT1a	63 (69.2)	65 (71.4)	
cT1b	28 (30.8)	26 (28.6)	
Imaging feature			0.532
GGO-dominant	58 (63.7)	62 (68.1)	
Solid-dominant	33 (36.3)	29 (31.9)	
Number of cases with systematic mediastinal nodal sampling, n (%)	54 (59.3)	87 (95.6)	<0.001
LN sampling number, n (range)	4 (0–7.5)	10 (6–14.5)	<0.001
Pathologic T stage, n (%)			0.158
pT1a	36 (39.6)	34 (37.4)	
pT1b	29 (31.9)	40 (44)	
pT2a [Vis PI]	26 (28.6)	17 (18.7)	
Pathologic N stage, n (%)			0.054
N0/Nx	90 (98.9)	85 (93.4)	
N1/2	1 (1.1)	6 (6.6)	
Histological differentiation			0.311
Grade I	51 (56.0)	57 (62.6)	
Grade II	28 (30.8)	28 (30.8)	
Grade III	12 (13.2)	6 (6.6)	

LN, lymph node.

In the current cohort, CTR, which can be considered an index of invasive component, was selected as one of prognostic factors by Cox proportional-hazards model. The correlation between CTR and their prognosis has been widely studied. Most previous studies reported that CTR is a significant prognostic factor in early NSCLC. Tsunezuka *et al.* reported that patients undergoing wedge resection with solid tumor size larger than 1.2 cm have a risk of recurrence (9). Tsutani *et al.* (21) reports that wedge resection has comparable surgical outcomes with segmentectomy for peripheral pulmonary nodules with CTR ≤0.5. However, Cho *et al.* (32) suggested that wedge resection should be cautiously performed for nodules with CTR >0.25, due to higher recurrence rate compared that nodules with CTR ≤0.25 (15.3% *vs.* 1.4%). Given that

lack of resection margin status and small sample size, the data from Choi's report have to be reconsidered with some skepticism. In this context, we excluded insufficient-margin cases and relatively large sample size were used over a short period of time to ensure homogeneity in treatment paradigms, staging, and practices.

Another prognostic factor of PFS in our cohort was MPNs, which has not been fully explored in previous studies. Yu *et al.* (33) compared the outcomes of patients with synchronous multiple primary lung cancers and solitary primary lung cancer (SMPLC). They found that tumor size was the only independent prognostic factor for SMPLC after surgical intervention. However, these findings are not comparable to the finding of the present study as the tumor size (tumors size ≥3 cm accounted for more than
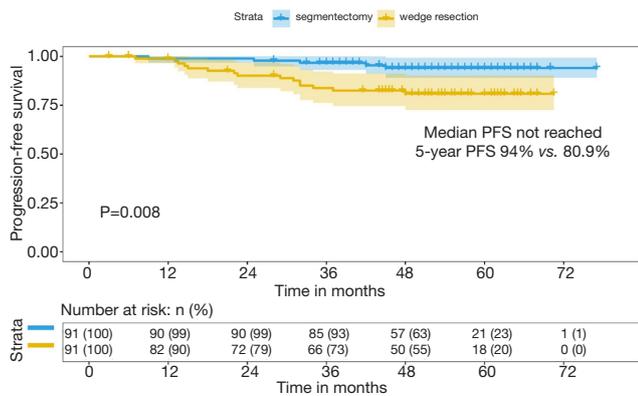
Figure 3 Progression-free survival of MPN patients underwent wedge resection and segmentectomy. Patients with MPN in segmentectomy group had better PFS than wedge resection group (94% *vs.* 80.9%, P=0.008). PFS, progression-free survival.

70%) was significantly larger than the tumor size of our cohort and the rate of sublobar resection was only 14.4%. The reason why MPNs had a worse PFS in our study may as follows: First, patients with MPNs had a longer period of follow-up than SPN, which may contribute to growth of main lesion and thus increase the invasive component. Second, diagnosis of multiple primary LUAD in the current cohort was mainly based on preoperative imaging features and pathological evaluation. Genomic analysis was not used for all multifocal nodules to differentiate metastases from multiple primaries. MPNs with solid component may metastasize through aerogenous spread (34), also referred as tumor spread through air spaces (STAS), which may affect tumor staging and management. Finally, since we performed synchronous multiple pulmonary wedge resections for MPNs and observed that the extent of main focus resection may be affected by other lesions. Therefore, wedge resection may not be effective and segmentectomy or lobectomy procedures may be more effective for MPN patients.

Our preliminary findings suggested that poor PFS of MPNs may be caused by surgical mode, therefore, we further compared wedge resection and segmentectomy procedures in patients with MPNs. Theoretically, patients with the same propensity score should have the same possibility of receiving wedge resection or segmentectomy. Therefore, results obtained using PSM method may increase the credibility of the conclusions and provide useful guidance (35). After PSM, Kaplan-Meier analysis showed that PFS of segmentectomy is significantly higher

compared with that of wedge resection in patients with MPNs. Several studies reported that segmentectomy should be the preferred technique for limited resection of patients with early-stage NSCLC (36,37). However, these studies did not take account of MPNs. In the current study, systematic mediastinal nodal sampling was performed in 95.6% of patients who underwent segmentectomy compared to only 59.3% of patients who had a wedge resection. This ratio is consistent with reports by Altorki *et al.* and the American College of Surgical Oncology Group (ACOSOG) Z4032 trial (20,38). Interestingly, both studies on small solitary tumor did not translate more lymph node assessment into more nodal upstaging or an improvement in OS or PFS. A reasonable explanation maybe that main focus in MPNs have a higher malignant potential compared with solitary lung tumor due to a longer follow-up period. Therefore, lower rate of nodal sampling may lead to occult metastases neglected, which would be reflected in lower rate of adjuvant chemotherapy received after surgery. In addition, segmentectomy were always carefully designed through three-dimensional reconstruction before surgeries. This would result to a better parenchymal resection margin compared to wedge resection. Therefore, more reasonable preoperational planning for limited resection in multifocal pulmonary adenocarcinoma should be emphasized and segmentectomy procedure is recommended.

The limitation of this study is its retrospective nature. First, as this study was designed as a single-center trial, it might not have the generalizability a multi-center trial typically retains. Second, the location of the main lesion and the number of nodules was not considered as a variable in patients with MPNs which might affect invasiveness and metastasis of lymph nodes and influence effectiveness of lymph node resection (39). Finally, the follow-up period for the cohort should be extended to obtain enough survival data. Further, randomized controlled trials should be carried out to evaluate the outcomes of MPN.

Conclusions

In summary, wedge resection is a practical option for appropriately selected early-stage adenocarcinoma, with tumor size less than 2 cm and a CTR ≤0.5. Multivariate analysis demonstrated that CTR and MPN are two independent prognostic factors affecting the surgical outcome of wedge resection. Therefore, for MPN which is not suitable for lobectomy, segmentectomy should be the surgical procedure of first choice. Regarding the lack of OS

in this study, we will continue to follow-up these patients for more than ten years to obtain conclusive results. In addition, further studies should be carried out to explore the appropriate surgical procedure for multifocal nodules.

Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at http://dx.doi.org/10.21037/jtd-20-3005

Data Sharing Statement: Available at http://dx.doi.org/10.21037/jtd-20-3005

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at http://dx.doi.org/10.21037/jtd-20-3005). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). This study was approved by ethics committee of National Cancer Center/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College (approval number: 191137-1921). The requirement of patients' informed consent was waived owing to the retrospective nature of the study.

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Table S1 Patients' clinicopathologic characteristics in SPN and MPN group

Clinicopathologic characteristic	SPN	MPN	P. value
Gender, n (%)			0.852
Male	35 (35.4)	31 (34.1)	
Female	64 (64.6)	60 (65.9)	
Age, y (range)	62 (50.5–72)	61 (53–66.5)	0.435
BMI	24.1 (22.2–26.9)	23.6 (21.9–25.6)	0.212
Smoking history, n (%)			0.997
No	74 (74.7)	68 (74.7)	
Yes	25 (25.3)	23 (25.3)	
Family history of carcinoma, n (%)			0.299
No	67 (67.7)	55 (60.4)	
Yes	32 (32.3)	36 (39.6)	
Tumor size (cm), n (%)	1.2 (0.9–1.5)	1.3 (1.05–1.6)	0.424
Clinical T stage, n (%)			0.944
cT1a	69 (69.7)	63 (69.2)	
cT1b	30 (30.3)	28 (30.8)	
Imaging features, n (%)			0.071
GGO-dominant	75 (75.8)	58 (63.7)	
Solid-dominant	24 (24.2)	33 (36.3)	
Number of cases with systematic mediastinal nodal sampling, n (%)	46 (46.5)	54 (59.3)	0.076
LN sampling number, n (range)	3 (0–7)	4 (0–7.5)	0.374
Pathologic T stage, n (%)			0.424
pT1a	48 (48.5)	36 (39.6)	
pT1b	29 (29.3)	29 (31.9)	
pT2a [Vis PI]	22 (22.2)	26 (28.6)	
Pathologic N stage, n (%)			0.952
N0/Nx	98 (99.0)	90 (98.9)	
N1/2	1 (1.0)	1 (1.1)	
Histological differentiation, n (%)			0.328
Grade I	65 (65.7)	51 (56.0)	
Grade II	26 (26.3)	28 (30.8)	
Grade III	8 (8.1)	12 (13.2)	

BMI, body mass index; GGO, ground-glass opacity; MPN, multiple pulmonary nodule; SPN, solitary pulmonary nodule; Vis PI, visceral pleura invasion.
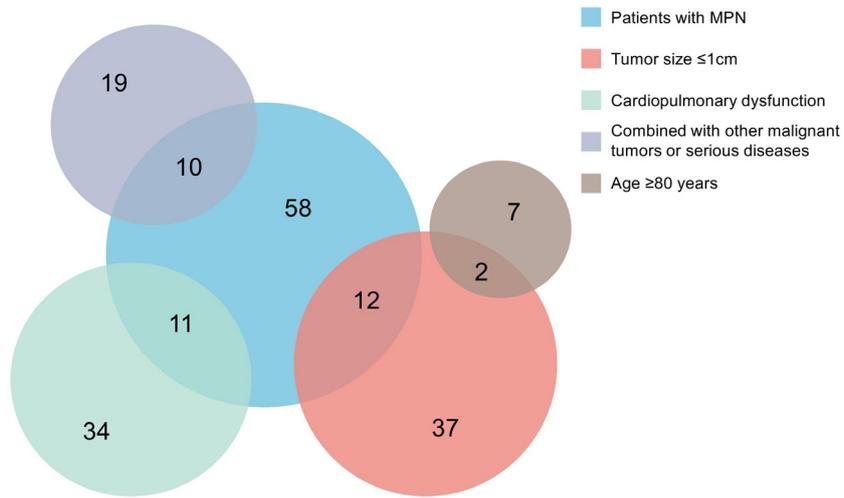
Figure S1 Venn diagram of indications for patients underwent wedge resection. MPN, multiple pulmonary nodule.
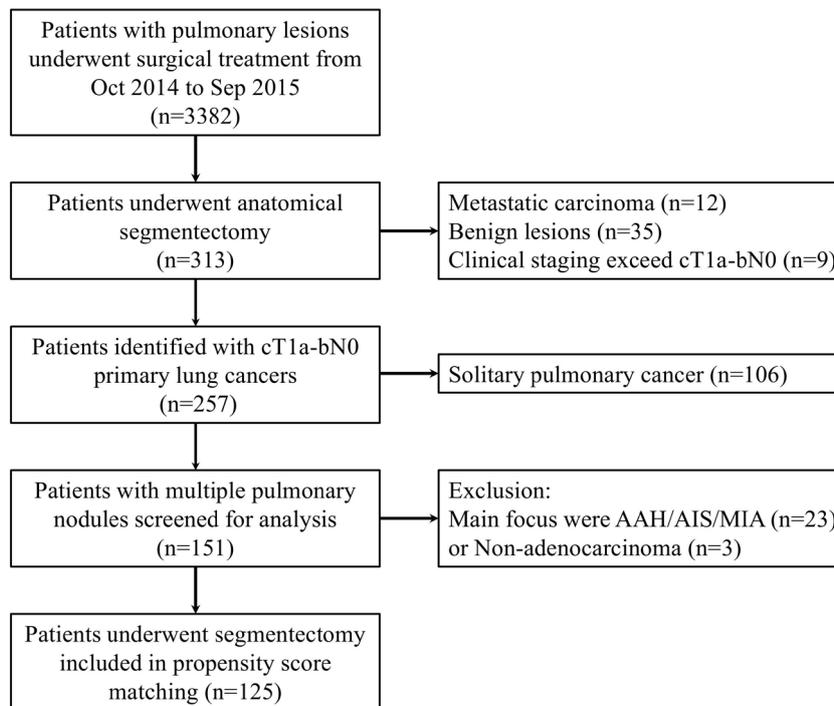

Figure S2 The flow diagram of the patient selection who underwent segmentectomy.

Table S2 The detail information of patients with tumor progression

Patients with tumor progression	Sex	Age	MPN/SPN	Imaging feature	Locations of recurrence or metastasis	Vis PI	MVI	Tumor size (cm)	Histological differentiation	Pathological subtype
1	Female	67	SPN	Solid-dominant	Pleural metastasis	Yes	No	1.7	Grade II	Mucinous adenocarcinoma
2	Male	68	SPN	Solid-dominant	Pleural metastasis	Yes	No	1.2	Grade II	Papillary
3	Male	77	SPN	Solid-dominant	Ipsilateral intrapulmonary metastasis	No	No	1.2	Grade III	Papillary
4	Female	64	SPN	Solid-dominant	Pleural metastasis	Yes	No	1.6	Grade II	Papillary
5	Male	51	SPN	Solid-dominant	Local recurrence	No	No	1.4	Grade I	Lepidic/Acinar
6	Female	71	MPN	GGO-dominant	Local recurrence	No	No	1.6	Grade I	Lepidic/Acinar
7	Male	57	MPN	Solid-dominant	Pleural metastasis	No	No	1.7	Grade II	Lepidic/Acinar
8	Female	69	MPN	Solid-dominant	Brain metastasis	Yes	No	1.3	Grade III	Lepidic/Acinar
9	Male	61	MPN	Solid-dominant	Local recurrence	Yes	Yes	1.8	Grade II	Micropapillary
10	Female	58	MPN	Solid-dominant	Mediastinal lymph node metastasis	Yes	Yes	1.6	Grade II	Micropapillary
11	Female	45	MPN	Solid-dominant	Local recurrence	No	No	1.5	Grade II	Lepidic/Acinar
12	Female	58	MPN	Solid-dominant	Mediastinal lymph node metastasis	No	Yes	0.9	Grade III	Micropapillary
13	Male	61	MPN	Solid-dominant	Adrenal metastases	Yes	No	1.6	Grade III	Lepidic/Acinar
14	Male	60	MPN	GGO-dominant	Local recurrence	No	No	1	Grade I	Lepidic/Acinar
15	Male	62	MPN	Solid-dominant	Local recurrence	No	No	1.3	Grade III	Lepidic/Acinar
16	Female	58	MPN	Solid-dominant	Bone metastasis	Yes	No	1.7	Grade II	Lepidic/Acinar
17	Female	79	MPN	Solid-dominant	Mediastinal lymph node metastasis	Yes	Yes	1.8	Grade III	Micropapillary
18	Male	82	MPN	Solid-dominant	Ipsilateral intrapulmonary metastasis	Yes	Yes	1.2	Grade III	Mucinous adenocarcinoma
19	Female	52	MPN	Solid-dominant	Mediastinal lymph node metastasis	Yes	No	1.8	Grade II	Lepidic/Acinar
20	Male	61	MPN	Solid-dominant	Pleural metastasis	Yes	No	1.5	Grade II	Papillary

MPN, multiple pulmonary nodule; MVI, microscopic vascular invasion; SPN, solitary pulmonary nodule; Vis PI, visceral pleura invasion.

Table S3 Baseline characteristics: wedge resection versus segmentectomy before propensity score matching

Variables	Wedge resection	Segmentectomy	P value
Age, y (range)	61 (53–66.5)	58 (53–65)	0.164
Female sex, n (%)	60 (65.9)	105 (74.5)	0.161
Tumor size, cm (range)	1.3 (1.05–1.6)	1.5 (1.2–1.9)	0.014
Clinical T stage, n (%)			0.044
cT1a	63 (69.2)	79 (56.0)	
cT1b	28 (30.8)	62 (44.0)	
Imaging feature			0.139
GGO-dominant	58 (63.7)	76 (53.9)	
Solid-dominant	33 (36.3)	65 (46.1)	
Number of cases with systematic mediastinal nodal sampling, n (%)	54 (59.3)	125 (88.7)	<0.001
LN sampling number, n (range)	4 (0–7.5)	10 (6–13)	<0.001
Pathologic T stage, n (%)			0.025
pT1a	36 (39.6)	57 (40.4)	
pT1b	29 (31.9)	63 (44.7)	
pT2a [Vis PI]	26 (28.6)	21 (14.9)	
Pathologic N stage, n (%)			0.053
N0/Nx	90 (98.9)	132 (93.6)	
N1/2	1 (1.1)	9 (6.4)	
Histological differentiation			0.131
Grade I	51 (56.0)	83 (58.9)	
Grade II	28 (30.8)	50 (35.5)	
Grade III	12 (13.2)	8 (5.7)	

LN, lymph node.