Ann Thorac Cardiovasc Surg 2017; 23: 291–297
Online October 2, 2017
doi: 10.5761/atcs.oa.17-00020

Original Article

Difference in Postsurgical Prognostic Factors between Lung Adenocarcinoma and Squamous Cell Carcinoma

Haruhiko Nakamura, MD, PhD, Hiroki Sakai, MD, Hiroyuki Kimura, MD, Tomoyuki Miyazawa, MD, Hideki Marushima, MD, PhD, and Hisashi Saji, MD, PhD

Purpose: The aim of this study was to compare the clinicopathologic prognostic factors between patients who underwent lung resection for adenocarcinoma (AD) and those with squamous cell carcinoma (SQ).
Methods: A database of patients with lung AD or SQ who underwent surgery with curative intent in our department from January 2008 to December 2014 was reviewed. Associations between various clinicopathologic factors, postsurgical recurrence-free survival (RFS), and overall survival (OS) were analyzed to find significant prognostic factors.
Results: A total of 537 lung cancer patients (AD, 434; SQ, 103) were included in this study. Although RFS was similar in patients with AD and SQ, OS was significantly poorer in those with SQ. Multivariate analysis in patients with AD revealed that age (≥69 vs. <69), lymphatic invasion, and histologic pleural invasion (p0 vs. p1–3) were associated with RFS, while gender and pleural invasion were associated with OS. In SQ, however, smoking, clinical stage, and pulmonary metastasis were associated with RFS in the multivariate analysis.
Conclusion: Since significant postoperative prognostic factors are quite different between lung AD and SQ, these two histologic types should be differently analyzed in a clinical study.

Keywords: adenocarcinoma, lung cancer, prognosis, squamous cell carcinoma, survival

Introduction

Lung adenocarcinoma (AD) and squamous cell carcinoma (SQ) are the two major histologic types of non-small-cell lung cancer (NSCLC), and have been considered to be almost similar in both postsurgical prognosis and chemotherapeutic responses for a long period of time. However, recent multiple studies on the postsurgical outcomes of these two histologic types indicate that overall survival (OS) is significantly better in AD when compared with SQ.[1,2] In addition, differences in certain chemotherapeutic responses have been reported; for instance, a chemotherapeutic regimen of cisplatin and gemcitabine was more effective for SQ, whereas, for AD, a regimen involving cisplatin and pemetrexed was found to be more effective.[3] In molecular-targeted therapy, the epidermal growth factor receptor tyrosine kinase inhibitors and anaplastic lymphoma tyrosine kinase inhibitors are known to be effective for the treatment of AD carrying activating mutations, but these mutations are rarely seen in SQ.[4–6] Epidemiologically, an increase in the prevalence of AD, particularly in the non-smoking population, and a decrease in SQ prevalence has been observed worldwide.[7,8] Therefore, in the present study, we analyzed the prognostic factors associated with the recently increasing ADs when compared with the decreasing SQs in the lung.

Department of Chest Surgery, St. Marianna University School of Medicine, Kawasaki, Kanagawa, Japan

Received: January 25, 2017; Accepted: June 1, 2017
Corresponding author: Haruhiko Nakamura, MD, PhD. Department of Chest Surgery, St. Marianna University School of Medicine, 2-16-1 Sugao, Miyamae-ku, Kawasaki, Kanagawa 216-8511, Japan
Email: h-nakamura@marianna-u.ac.jp

Table 1 Clinicopathological factors in lung adenocarcinoma and squamous cell carcinoma

Factors		AD	SQ	$P^{\dagger}$
Clinical factors				
Sex	M	220	91	
	F	214	12	<0.0001*
Age (years)		68 ± 9	70 ± 7	0.1863
Smoking	Smoker	245	98	
	Never-smoker	189	5	<0.0001*
Smoking index‡		438 ± 554	1113 ± 654	<0.0001*
Tumor size (mm)		29 ± 13	37 ± 18	<0.0001*
PET/SUVmax**		3.1 ± 3.4	7.5 ± 5.2	<0.0001*
Clinical stage	IA + IB	388	79	
	≥IIA	46	24	0.0006*
Surgical methods	Sublobar resection	151	42	
	Lobectomy	277	58	
	Pneumonectomy	3	1	
	Combined resection	3	2	0.3812
Pathologic factors				
Ly	ly0	370	75	
	ly1	64	28	0.0026*
V	v0	386	78	
	v1–2	48	25	0.0005*
P	p0	347	76	
	p1–3	87	27	0.1688
Pm	pm0	421	100	
	pm1–2	13	3	0.9646
Pathologic stage§	IA + IB	271	57	
	≥IIA	26	4	0.3180

AD: adenocarcinoma; SQ: squamous cell carcinoma; M: male; F: female; SD: standard deviation; PET: positron emission tomography; SUV: standardized uptake value; Ly: lymphatic invasion; V: venous invasion; P: pleural invasion; Pm: pulmonary metastasis; †Chi-square test for categorical variables and Mann–Whitney U-test for continuous variables; ‡Cigarettes/day × years; **112 cases were excluded because preoperative PET/CT was not performed; §179 cases were excluded because of limited resection without systematic lymph node dissection; continuous variables are shown by mean ± SD; *Statistically significant values

Patients and Methods

Patients

This retrospective study was approved by the Institutional Review Board of the St. Marianna University School of Medicine. A clinicopathologic database of patients with AD or SQ of the lung who underwent surgery with curative intent in our department from January 2008 to December 2014 was reviewed. Records were obtained and the surgical methods used for treatment were classified into the following four types: sublobar resection (wedge resection or segmentectomy), lobectomy (including bilobectomy), pneumonectomy, and combined lung resection with adjacent organs. Bronchial or tracheal resections without lung resection, patients with multiple lung cancers and different histologic types, and those who received preoperative induction therapy were excluded. Disease stages were determined according to the international staging criteria for lung cancer, published by the American Joint Committee on Cancer/Union for International Cancer Control/International Association for the Study of Lung Cancer in 2009.[9)]

Statistical analysis

Categorical variables for contingency tables were tested using the chi-square test, whereas continuous variables in multiple groups were tested using the Kruskal–Wallis test. Estimated survival rates after surgery were calculated using the Kaplan–Meier method, and survival differences between patient groups were tested using the log-rank test. The cox proportional hazard model was used for multivariate analysis of postsurgical survival. P <0.05 was considered as significant.

Table 2 Univariate analysis for recurrence-free survival and overall survival in lung adenocarcinoma

Factors		N	5-year RFS (%)	$P^{\dagger}$	5-year OS (%)	$P^{\dagger}$
Sex	M	214	72.3		81.8	
	F	220	85.5	0.0220*	96.3	0.0006*
Age (years)	≥69	233	70.0		83.4	
	<69	201	88.8	0.0034*	94.8	0.0156*
Smoking	Smoker	245	76.3		83.9	
	Never-smoker	189	81.8	0.347	94.6	0.0111*
Tumor size	>2 cm	307	74.7		88.7	
	≤2 cm	127	88.3	0.0109*	89.8	0.272
PET/SUV max**	≥3.0	133	55.4		76.2	
	<3.0	208	88.9	<0.0001*	94.8	<0.0001*
Clinical stage	c-IA + IB	388	80.7		89.9	
	≥c-IIA	46	59.5	0.0013*	79.2	0.0282*
Ly	ly0	370	85.8		90.7	
	ly1	64	44.2	<0.0001*	78.3	0.0075*
V	v0	336	83.8		91.0	
	v1–2	48	43.6	<0.0001*	70.9	<0.0001*
P	p0	347	83.4		93.2	
	p1–3	87	58.8	<0.0001*	68.3	<0.0001*
Pm	pm0	421	80.4		89.9	
	pm1–2	13	32.8	<0.0001*	53.6	0.0003*
Pathological stage§	p-IA + IB	271	85.6		93.3	
	≥p-IIA	26	29.0	<0.0001*	55.5	<0.0001*

N: number of patients; RFS: recurrence-free survival; OS: overall survival; M: male; F: female; PET: positron emission tomography; SUV: standardized uptake value; Ly: lymphatic invasion; V: venous invasion; P: pleural invasion; Pm: pulmonary metastasis; †log-rank test; **93 cases were excluded because preoperative PET/CT was not performed; §137 cases were excluded because of limited resection without systematic lymph node dissection; *Statistically significant values

Results

A total of 537 patients (434 ADs and 103 SQs) comprising 311 males and 226 females with a mean age of 69 ± 9 years (range, 22–89 years) were included in this study. The mean postoperative follow-up period was 29 ± 21 months (range, 1–82 months). **Table 1** demonstrates the differences in clinicopathologic factors between AD and SQ patients. Significant differences were found in sex distribution, smoking habit, tumor size, maximum standardized uptake value in positron emission tomography (PET/SUVmax), clinical stage, lymphatic invasion, and venous invasion.

Although postsurgical 5-year recurrence-free survival (RFS) was similar in patients with AD (78.9%) and SQ (74.5%; $P = 0.2126$), the 5-year OS was significantly better in those with AD when compared with SQ (88.9% vs. 68.4%; $P = 0.0002$), suggesting that deaths from diseases other than lung cancer were frequent in patients with SQ. Similar results were observed in AD (n = 268) and SQ (n = 41) patients with clinical stage IA tumors, wherein the 5-year RFS was 87.8% and 88.3% ($P = 0.8500$), and the 5-year OS was 92.3% and 60.5% ($P = 0.0008$) in the AD and SQ patients, respectively.

Various clinicopathologic factors were significantly associated with RFS and OS in patients with AD in the univariate analysis (**Table 2**). In the multivariate analysis including all the significant factors found in the univariate analysis, age (≥69 vs. <69) and lymphatic invasion were found to be associated with RFS, sex was found to be associated with OS, and histologic pleural invasion (p0 vs. p1–3) was observed to be associated with both RFS and OS (**Table 3**). In contrast, fewer factors were significantly associated with RFS and OS in patients with SQ in the univariate analysis (**Table 4**). Smoking, clinical stage, pulmonary metastasis, and pathologic stage were associated with RFS and pulmonary metastasis alone was significantly associated with OS. Finally, smoking, clinical stage, and pulmonary metastasis were associated with RFS in the multivariate analysis (**Table 5**). In this multivariate analysis, pathologic stage was excluded from the analysis because of multicollinearity between pathologic stage and clinical stage.

Table 3 Multivariate analysis using the Cox proportional hazard model for recurrence-free survival and overall survival in 242 patients with lung adenocarcinoma

Factor	HR (95% CI) in RFS	$P^{\dagger}$	HR (95% CI) in OS	$P^{\dagger}$
Sex (M vs. F)	1.085 (0.562–2.092)	0.8093	3.774 (1.032–13.89)	0.0446*
Age (≥69 vs. <69)	2.568 (1.278–5.162)	0.0081*	1.962 (0.733–5.249)	0.1794
Smoking (smoker vs. never-smoker)	NA		2.036 (0.627–6.607)	0.2364
Tumor size (<2 cm vs. ≤2 cm)	1.019 (0.313–3.317)	0.9751	NA	
PET/SUVmax (≥3.0 vs. <3.0)	2.392 (0.994–5.747)	0.0516	1.934 (0.560–6.667)	0.2970
Clinical stage (≥stage IIA vs stage IA + B)	1.063 (0.407–2.776)	0.9000	1.262 (0.355–4.486)	0.7194
Ly (ly1 vs. ly0)	3.096 (1.342–7.143)	0.0080*	0.8576 (0.2107–3.497)	0.8305
V (v1–2 vs. v0)	1.105 (0.472–2.591)	0.8179	2.004 (0.5402–7.463)	0.2984
P (p1–3 vs. p0)	2.331 (1.112–4.878)	0.0248*	3.300 (1.139–9.524)	0.0278*
Pm (pm1–2 vs. pm0)	1.412 (0.415–4.808)	0.5804	1.631 (0.3182–8.403)	0.5571
Pathologic stage (≥stage IIA vs stage IA + B)	2.123 (0.945–4.762)	0.0681	2.591 (0.670–10.00)	0.1675

HR: hazard ratio; CI: confidence interval; RFS: recurrence-free survival; OS: overall survival; M: male; F: female; NA: not applicable; PET: positron emission tomography; SUV: standardized uptake value; Ly: lymphatic invasion; V: venous invasion; P: pleural invasion; Pm: pulmonary metastasis; †Cox proportional hazard model; *Statistically significant values

Table 4 Univariate analysis for recurrence-free survival and overall survival in lung squamous cell carcinoma

Factors		N	5-year RFS (%)	$P^{\dagger}$	5-year OS (%)	$P^{\dagger}$
Sex	M	91	72.8		63.4	
	F	12	87.5	0.3739	100	NA
Age (years)	≥69	63	75.6		63	
	<69	40	73	0.7690	75.2	0.2850
Smoking***	Smoker	98	76.9		67.7	
	Never-smoker	5	0	0.0061*	NR	NA
Tumor size	>2 cm	87	70.6		66	
	≤2 cm	16	92.3	0.1302	76.4	0.3223
PET/SUVmax**	≥3.0	74	74.3		74.3	
	<3.0	10	76.2	0.8512	65.6	0.9344
Clinical stage	c-IA + IB	79	80.4		68.6	
	≥c-IIA	24	NR	0.0005*	72.1	0.5670
Ly	ly0	75	75.3		71.8	
	ly1	28	72.6	0.5893	58.1	0.5799
V	v0	78	76.2		71.8	
	v1–2	25	68.9	0.2898	56.2	0.1190
P	p0	76	78.9		69.8	
	p1–3	27	60.7	0.1077	66.5	0.3957
Pm***	pm0	100	75.2		69.2	
	pm1–2	3	NR	0.0007*	NR	0.0012*
Pathologic stage§	p-IA + IB	57	80.8		68.4	
	≥p-IIA	4	25	0.0011*	33.3	0.1807

N: number of patients; RFS: recurrence-free survival; OS: overall survival; M: male; F: female; PET: positron emission tomography; SUV: standardized uptake value; Ly: lymphatic invasion; V: venous invasion; P: pleural invasion; Pm: pulmonary metastasis; NR: not reached; NA: not applicable since no event was observed in one of the compared groups; †log-rank test; **19 cases were excluded because preoperative PET/CT was not performed; §42 cases were excluded because of limited resection without systematic lymph node dissection; *Statistically significant values; ***Extreme imbalance existed between the compared groups.

Discussion

In the present study, remarkable clinicopathologic differences were observed between the AD and SQ patients. The majority (90%) of patients with SQ were males and are thought to possess sex-related risk factors for OS because it is well known that life expectancy is shorter in males than in females in most countries. The prognosis of NSCLC has been found to be significantly poor in males than in females in several Japanese nationwide

Table 5 Multivariate analysis using the Cox proportional hazard model for recurrence-free survival in 103 patients with lung squamous cell carcinoma

Factor	HR (95% CI) in RFS	$P^{\dagger}$
Smoking (smoker vs. never-smoker)	0.124 (0.025–0.607)	0.0100*
Clinical stage (≥ stage IIA vs stage IA + B)	5.423 (2.055–14.32)	0.0006*
Pm (pm1–2 vs. pm0)	22.73 (1.890–250)	0.0138*

HR: hazard ratio; CI: confidence interval; RFS: recurrence-free survival; Pm: pulmonary metastasis; †Cox proportional hazard model; *Statistically significant values.

surveillances regarding postsurgical OS in lung cancer, performed every 5 years by the Japanese Joint Committee for Lung Cancer Registration (JJCLCR).[10] Thus, one of the reasons for the poor prognosis in SQ patients may be attributed to the higher percentage of males in this study. Furthermore, the development of SQ is closely associated with tobacco smoking. The present study demonstrated that 95% of patients with SQ were current or past smokers. The smoking habit is associated with several life-threatening diseases such as lung emphysema, pneumonia, ischemic heart diseases, brain infarction, and several malignant tumors including lung cancer,[11] which may worsen the OS in patients with SQ when compared to those with AD. Moreover, larger tumor size, higher SUVmax at the primary lesion, and increased lymphatic and venous invasions in patients with SQ demonstrates the typical local invasive nature of SQ when compared with AD. The RFS did not differ between the AD and SQ patients, when limited to those with c-stage IA, which indicates that the biologic malignant grades of these two histologic types might be comparable as a whole. Although many significant prognostic factors in AD were found in the univariate analysis in both RFS and OS, fewer prognostic factors were found in SQ. Some of these findings are similar to those found in a JJCLCR report, wherein females with pathologic stage I/II AD had a significantly better prognosis than males, but there was no significant prognostic difference between non-AD male and female patients with pathologic stage I/II disease.[10] In our present study, male sex and higher age were worse prognostic factors for RFS in AD patients in the univariate analysis, suggesting these factors might be associated with biologic malignant grade of the tumor. Similar results in NSCLC were reported from other institutions.[12,13]

Various factors such as age, sex, smoking habit, ethnicity, tumor size, SUVmax, visceral pleural invasion, lymphatic invasion, and venous invasion have been reported to predict survival in surgical cases of NSCLC.[14–25] However, only a few reports have analyzed AD and SQ separately. In the present study, the most powerful prognostic factors for RFS and OS in AD were histologic pleural invasion. In our previous studies, we had reported that SUVmax 3.0 in the primary lesion was useful to identify node-negative patients[25] and to select patients suitable for limited lung resection in NSCLC.[26] However, SUVmax was only marginally significant (P = 0.0516) for RFS in AD in multivariate analysis in the present study. Multiple studies have shown that SUVmax is a significant prognostic factor in NSCLC.[24,27,28] However, one study revealed a statistically significant correlation between SUVmax and prognosis in patients with AD, but not SQ,[29] and also reported that other clinicopathologic factors did not have a role in predicting OS in patients with SQ. In another study, venous invasion was significantly associated with RFS in patients with AD but not SQ.[22] Interestingly, the results of the present study are in accordance with the findings of these two studies. In SQ, multivariate analysis revealed that smoking, clinical stage, and pulmonary metastasis were significant prognostic factors for RFS. However, these results should be cautiously interpreted because extreme imbalance existed between the compared groups in non-smoker and pulmonary metastasis due to small number of patients.

Conclusion

In conclusion, higher percentages of smokers and male patients with lung SQ were speculated to have shorter OS when compared to AD. Various significant prognostic factors were found in patients with AD in univariate analysis, whereas fewer factors were predictive in SQ. Since significant postoperative prognostic factors are quite different between lung AD and SQ, these two histologic types should be differently analyzed in a clinical study.

Disclosure Statement

There are no conflicts of interest to be declared.

References

1) Asamura H, Goya T, Koshiishi Y, et al. A Japanese lung cancer registry study: prognosis of 13,010 resected lung cancers. J Thorac Oncol 2008; **3**: 46-52.
2) Sawabata N, Miyaoka E, Asamura H, et al. Japanese lung cancer registry study of 11,663 surgical cases in 2004: demographic and prognosis changes over decade. J Thorac Oncol 2011; **6**: 1229-35.
3) Scagliotti GV, Parikh P, von Pawel J, et al. Phase III study comparing cisplatin plus gemcitabine with cisplatin plus pemetrexed in chemotherapy-naive patients with advanced-stage non-small-cell lung cancer. J Clin Oncol 2008; **26**: 3543-51.
4) Lynch TJ, Bell DW, Sordella R, et al. Activating mutations in the epidermal growth factor receptor underlying responsiveness of non-small-cell lung cancer to gefitinib. N Engl J Med 2004; **350**: 2129-39.
5) Paez JG, Jänne PA, Lee JC, et al. EGFR mutations in lung cancer: correlation with clinical response to gefitinib therapy. Science 2004; **304**: 1497-500.
6) Kwak EL, Bang YJ, Camidge DR, et al. Anaplastic lymphoma kinase inhibition in non-small-cell lung cancer. N Engl J Med 2010; **363**: 1693-703.
7) Charloux A, Quoix E, Wolkove N, et al. The increasing incidence of lung adenocarcinoma: reality or artefact? A review of the epidemiology of lung adenocarcinoma. Int J Epidemiol 1997; **26**: 14-23.
8) Devesa SS, Bray F, Vizcaino AP, et al. International lung cancer trends by histologic type: male:female differences diminishing and adenocarcinoma rates rising. Int J Cancer 2005; **117**: 294-9.
9) Vallières E, Shepherd FA, Crowley J, et al. The IASLC lung cancer staging project: proposals regarding the relevance of TNM in the pathologic staging of small cell lung cancer in the forthcoming (seventh) edition of the TNM classification for lung cancer. J Thorac Oncol 2009; **4**: 1049-59.
10) Sakurai H, Asamura H, Goya T, et al. Survival differences by gender for resected non-small cell lung cancer: a retrospective analysis of 12,509 cases in a Japanese lung cancer registry study. J Thorac Oncol 2010; **5**: 1594-601.
11) Doll R, Peto R, Wheatley K, et al. Mortality in relation to smoking: 40 years' observations on male British doctors. BMJ 1994; **309**: 901-11.
12) Fukumoto K, Taniguchi T, Usami N, et al. The ABO blood group is an independent prognostic factor in patients with resected non-small cell lung cancer. J Epidemiol 2015; **25**: 110-6.
13) Qiang G, Liang C, Xiao F, et al. Impact of chronic obstructive pulmonary disease on postoperative recurrence in patients with resected non-small-cell lung cancer. Int J Chron Obstruct Pulmon Dis 2015; **11**: 43-9.
14) Fujisawa T, Iizasa T, Saitoh Y, et al. Smoking before surgery predicts poor long-term survival in patients with stage I non-small-cell lung carcinomas. J Clin Oncol 1999; **17**: 2086-91.
15) Ou SH, Ziogas A, Zell JA. Asian ethnicity is a favorable prognostic factor for overall survival in non-small cell lung cancer (NSCLC) and is independent of smoking status. J Thorac Oncol 2009; **4**: 1083-93.
16) Kawaguchi T, Matsumura A, Fukai S, et al. Japanese ethnicity compared with Caucasian ethnicity and never-smoking status are independent favorable prognostic factors for overall survival in non-small cell lung cancer: a collaborative epidemiologic study of the National Hospital Organization Study Group for Lung Cancer (NHSGLC) in Japan and a Southern California Regional Cancer Registry databases. J Thorac Oncol 2010; **5**: 1001-10.
17) Nakamura H, Ando K, Shinmyo T, et al. Female gender is an independent prognostic factor in non-small-cell lung cancer: a meta-analysis. Ann Thorac Cardiovasc Surg 2011; **17**: 469-80.
18) Kudo Y, Saji H, Shimada Y, et al. Impact of visceral pleural invasion on the survival of patients with non-small cell lung cancer. Lung Cancer 2012; **78**: 153-60.
19) Wang J, Wang B, Zhao W, et al. Clinical significance and role of lymphatic vessel invasion as a major prognostic implication in non-small cell lung cancer: a meta-analysis. PLoS ONE 2012; **7**: e52704.
20) Nentwich MF, Bohn BA, Uzunoglu FG, et al. Lymphatic invasion predicts survival in patients with early node-negative non-small cell lung cancer. J Thorac Cardiovasc Surg 2013; **146**: 781-7.
21) Tao H, Hayashi T, Sano F, et al. Prognostic impact of lymphovascular invasion compared with that of visceral pleural invasion in patients with pN0 non-small-cell lung cancer and a tumor diameter of 2 cm or smaller. J Surg Res 2013; **185**: 250-4.
22) Usui S, Minami Y, Shiozawa T, et al. Differences in the prognostic implications of vascular invasion between lung adenocarcinoma and squamous cell carcinoma. Lung Cancer 2013; **82**: 407-12.
23) Warwick R, Shackcloth M, Mediratta N, et al. Female sex and long-term survival post curative resection for non-small-cell lung cancer. Eur J Cardiothorac Surg 2013; **44**: 624-30.
24) Yoo IeR, Chung SK, Park HL, et al. Prognostic value of SUVmax and metabolic tumor volume on 18F-FDG PET/CT in early stage non-small cell lung cancer patients without LN metastasis. Biomed Mater Eng 2014; **24**: 3091-103.
25) Nakamura H, Saji H, Marushima H, et al. Standardized uptake values in the primary lesions of non-small-cell lung cancer in FDG-PET/CT can predict regional lymph node metastases. Ann Surg Oncol 2015; **22**: S1388-93.
26) Nakamura H, Saji H, Marushima H, et al. Glucose uptake values in positron emission tomography are useful to predict survival after sublobar resection for lung cancer. Thorac Cardiovasc Surg 2017; **65**: 150-157.

27) Ohtaki Y, Shimizu K, Kaira K, et al. Risk factors associated with recurrence of surgically resected node-positive non-small cell lung cancer. Surg Today 2016; **46**: 1196-208.
28) Konings R, van Gool MH, Bard MP, et al. Prognostic value of pre-operative glucose-corrected maximum standardized uptake value in patients with non-small cell lung cancer after complete surgical resection and 5-year follow-up. Ann Nucl Med 2016; **30**: 362-8.
29) Shimizu K, Maeda A, Yukawa T, et al. Difference in prognostic values of maximal standardized uptake value on fluorodeoxyglucose-positron emission tomography and cyclooxygenase-2 expression between lung adenocarcinoma and squamous cell carcinoma. World J Surg Oncol 2014; **12**: 343.