RESEARCH ARTICLE

Postoperative survival According to the Glasgow Prognostic Score in Patients with Resected Lung Adenocarcinoma

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Abstract

Background: The Glasgow Prognostic Score (GPS) is calculated from measured CRP and albumin levels. We here evaluated the significance of the GPS in patients with resected pulmonary adenocarcinoma. **Materials and Methods:** The present study included 156 patients with lung adenocarcinoma who underwent lobectomy at Kanazawa Medical University between 2002 and 2012. Classification was into three groups: those with normal albumin (>=3.5 g/dl) and C-reactive protein (CRP) (<=1.0 mg/dl) levels were classified as GPS 0 (n =136), those with low albumin (<3.5 g/dl) or elevated CRP (>1.0 mg/dl) levels as GPS 1 (n = 16), and those with low albumin (<3.5 g/dl) and elevated CRP (>1.0 mg/dl) levels as GPS 2 (n = 4). We retrospectively investigated relationships between the patient characteristics including the GPS, and disease-free survival and cancer-specific survival. **Results:** The pathological stages of the patients were as follows: IA (n=78, 50%), IB (n=31, 19.9%), IIA (n=20.0, 12.8%), IIB (n=9.0, 5.7%), and IIIA (n=18.0, 11.5%). Lobectomy was performed in all cases. The average GPS was 0.15 (0-2) and showed significant relationships with stage and tumor size. The 2-year survival rates in patients with GPS0, 1 and 2 were 81.4%, 38.4%, and 25.0%, respectively. Clear correlations were noted with both cancer-specific survival and disease-free survival. Furthermore, multivariate analysis revealed that GPS was a significant prognostic factor. **Conclusions:** The GPS could be a prognostic factor for patients with resected pulmonary adenocarcinoma.

Keywords: : Lung adenocarcinoma- glasgow prognostic score- prognosis

Introduction

Lung cancer is the leading cause of cancer-related death worldwide (Jemal A et al., 2011). Lung adenocarcinoma, the most common type of primary lung cancer, is diagnosed in 1 million patients each year (Siegel R et al., 2014). Targeted therapy has been successful in a subset of lung adenocarcinoma patients with driver oncogenic mutations (Lynch TJ et al., 2004). However, the effect is still insufficient, and lung adenocarcinoma is still associated with a high rate of mortality.

Studies have found that the prognosis of cancer is related to inflammation (Mei Z et al., 2014). Inflammation-based prognostic scores have been developed to predict the prognosis of cancer patients. The Glasgow Prognostic Score (GPS), which is based on serum albumin and C-reactive protein (CRP) levels, is the most commonly used scoring system (Al Murri AM et al., 2006). Recently, the GPS has been reported to be a prognostic factor for patients with cancer (Mimatsu K et al., 2014: La Torre M et al., 2012: Horino K et al., 2013: Vashist YK et al., 2011). An elevated GPS has been shown to be associated with a worse prognosis in patients

with inoperable non-small cell lung cancer (NSCLC) (Forrest LM et al., 2003: Forrest LM et al., 2005). Furthermore, Tomita et al. reported that the preoperative GPS may be useful to predict the prognosis of patients with NSCLC (Tomita M et al., 2014); however, the report did not focus patients with lung adenocarcinoma, which is relatively homogeneous group. We therefore examined postoperative survival, according to the GPS, in patients with resected pulmonary adenocarcinoma.

Materials and Methods

Patients

We retrospectively reviewed a database of 156.0 continuous patients (75.0 men and 81.0 women) who underwent lobectomy at Kanazawa Medical University between 2002 and 2012. All patients underwent pulmonary lobectomy and had histologically-confirmed primary pulmonary adenocarcinomas. Tumors were classified according to the TNM classification (7th edition) (Goldstraw P et al., 2007). The study was approved by the Institutional Review Board of Kanazawa Medical University, Ishikawa, Japan (I045).

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Measurement of Glasgow prognostic score

The blood sample collection was performed on admission. The GPS definitions were as follows: Patients with a CRP level of < 10 mg/L and an albumin level of >35 g/L were allocated to GPS 0. If only the CRP was increased or the albumin level was decreased, the patients were allocated to GPS1. The patients in whom the CRP level was >10 mg/L and the albumin level was <35 g/L were classified as GPS 2. This study is a retrospective design.

Statistical analysis

The prognostic factors were examined using both univariate and multivariate analyses. The disease-free survival (DFI) rates and overall survival (OS) rates were calculated using the Kaplan-Meier method and compared using the log-rank test. Hazard ratios and confidence intervals were estimated with the use of a stratified Cox proportional-hazards model. P values of <0.05 were considered to indicate statistically significance. All statistical analyses were performed using the StatView software program (SAS Institute Inc, Cary, NC).

Results

The baseline patient characteristics are shown in Table 1. The median age of the patients was 65.2 years (range: 31-83). The GPS of the study patients were as follows: GPS0 (n=136, 87.2%), GPS1 (n=16, 10.3%), and GPS2 (n=4.0, 2.5%). Seventy-five patients (48.1%) were male and Eighty-nine patients (57.1%) were smokers. The pathological stages of the patients were as follows: IA (n=78, 50%), IB (n=31, 19.9%), IIA (n=20, 12.8%), IIB (n=9, 5.7%), IIIA (n=18.0, 11.5%). Forty-nine (31.4%) patients had comorbidities. Relationships between GPS and clinicopathological features of the patients are shown in Table 2. Stage and tumor size show significant relationship with GPS.

The 5-year survival rates of patients with GPS 0, 1 and 2 were 86.7%, 56.3% and 25%, respectively (Figure 1). The 5-year survival rates of GPS 1/2 was significant .

The median follow-up period of the survivors was 48.0 months. During the follow-up period, 33 (21.2%) patients died. A Kaplan-Meyer method revealed a significant association between the GPS and the disease-free survival (p=0.001) (Figure 2), and overall survival (p<0.001)
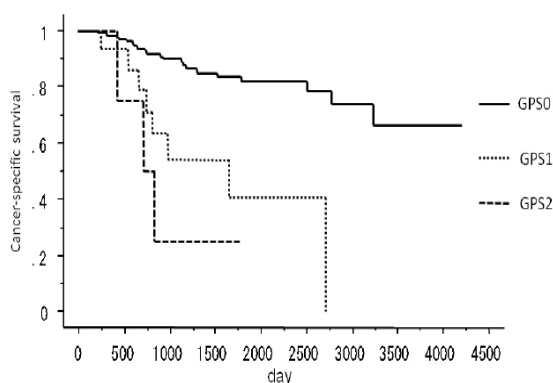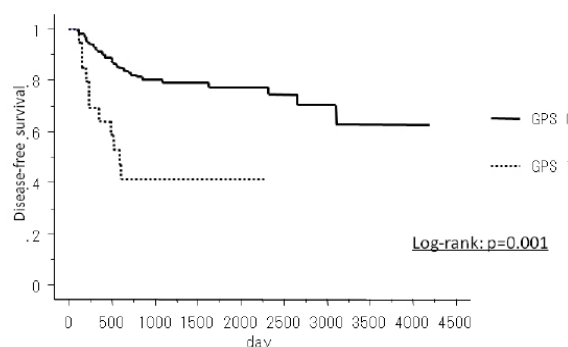
Figure 2. The Disease-Free Survival of GPS0 and GPS1/2 in Lung Adenocarcinoma Patients

(Figure 3). Gender (p=0.011), Smoking (p<0.001), Tumor size (p=0.001), Lymph node metastasis (p<0.001), Differentiation (G3/4) (p=0.047) and GPS (p<0.001) were significantly associated with cancer-specific survival in a univariate analysis (Table 3). The multivariate analysis of these significant variables showed the GPS (HR: 2.9 95% CI: 1.25 -6.67 p=0.013), smoking and tumor size to be independently associated with cancer-specific survival (Table 4).

Discussion

Many cancers arise from sites of infection, chronic irritation and inflammation (Coussens LM et al., 2002). The association between inflammation and lung cancer has been extensively reported (Tauler J et al., 2009). Recently, There are reports about the relationship between the GPS and resected lung cancer (Tomita M et al., 2014: Miyazaki T et al., 2015). However,

Table 1. The Patients' Characteristics

		No. of Patients	%
Age	>=65	86	55.1
	<65	70	44.9
Gender	male	75	48.1
	female	81	51.9
Smoking	+	89	57.1
	-	67	42.9
Stage	IA	78	50.0
	IB	31	19.9
	IIA	20	12.8
	IIB	9	5.7
	IIIA	18	11.5
Tumor Size	>=3.0cm	57	36.5
	<3.0cm	99	63.5
LN metastasis	+	33	21.2
	-	123	78.8
Differentiation	1.2	142	91.0
	3.4	14	9.0
GPS	0.0	136	87.2
	1.0	16	10.3
	2.0	4	2.5

Figure 1. The Cancer-Specific Survival of GPS0, 1 and 2 in Lung Adenocarcinoma Patients
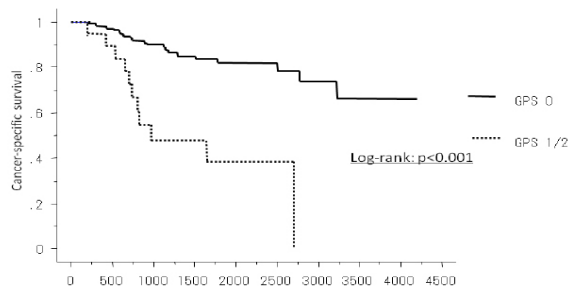
Figure 3. The Cancer-Specific Survival of GPS0 and GPS1/2 in Lung Adenocarcinoma Patients

there are no reports on relationship between GPS and resected lung adenocarcinoma. We therefore investigated the relationship between the GPS and resected lung adenocarcinoma.

The GPS was found to be correlated with the Stage and tumor size in the present study. Cancer progression releases inflammatory cytokines and growth factors. These are increased as part of the systemic inflammatory response (Canna K et al., 2008) and lead to the production of CRP. When the inflammatory reaction advances, the systemic nutritional status worsens, and the albumin value decreases. Thus, the GPS seemed to be related to the progression, which is reflected by the stage and tumor size. Because GPS may be involved to the LN factor , the LN factor was not associated in survival by multivariable analysis.

In the present study, we found that the GPS predicted the prognosis as well as the pathological stage of 156.0 patients who underwent lobectomy for adenocarcinoma. The GPS was associated significantly shorter disease-free survival rates and overall survival in resected lung adenocarcinoma. Moreover, a multivariate analysis revealed that the GPS was a significant prognostic factor for overall survival. Our findings suggest that, similar to other cancers, the GPS could be a very important factor for predicting the prognosis of patients with resected adenocarcinoma of the lung. However, the results should be interpreted with caution because the present study involved a short observation period and a small number of cases.

Recently, in NSCLS, it was reported that GPS were positive correlatived with cytokeratin 19 fragment antigen 21-1(CYFRA21-1), carcinoembryonic antigen (CEA) and tissue polypeptide specific antigen (TPS) in patients with advanced NSCLS (Jiang AG et al., 2015). GPS of score

Table 2. Clinicopathological Characteristics of Study Participants

		GPS0	GPS1/2	p value
Gender	male	62	13	0.167
	female	74	7	
Smoking	+	81	8	0.159
	-	55	12	
Age	>=65	72	14	0.234
	<65	64	6	
Stage	I	102	7	0.001
	II/IIIA	34	13	
Tumor size	>=3cm	45	12	0.037
	< 3cm	91	8	
LN metastasis	+	25	8	0.055
	-	111	12	
Differentiation	1.2	124	18	1.000
	3.4	10	2	

2 predicts a prolonged ICU stay in patients undergoing pneumonectomy (Petrella F et al., 2016). Furthermore, in the other cancers, the presence of a systemic inflammatory response, as evidenced by the GPS, appears to be superior to the subjective assessment of a patient's performance status (PS) in predicting the response to platinum-based chemotherapy in patients with advanced gastroesophageal cancer (Crumley AB et al., 2008). The GPS was also found to be an independent negative prognostic factor for overall survival in esophageal cancer patients treated with the combination chemotherapy of docetaxel and nedaplatin as a second-line chemotherapy (Kawabata R et al., 2011). We therefore suggest that the GPS is useful index that is simple and easy to implement in the clinical setting, not only surgery cases but also in chemotherapy cases. These characteristics will make the GPS an important index for various fields.

This study has same limitations. This study is retrospective design. In future, prospective study will be necessary. In conclusion, the GPS was demonstrated to be correlated with poor survival. The GPS is therefore important in predicting the prognosis of lung adenocarcinoma.

Conflict of interest

The authors declare no conflicts of interest in association with this study.

Table 3. A Univariate Survival Analysis Examining the Association between the Glasgow Prognostic Scores (GPS) and Survival

Parameter	HR	95% CI	P value
Age(>=65)	1.5	0.7-3.1	0.249
Gender	0.4	0.2-0.8	0.011
Smoking	3.9	1.8-8.3	<0.001
Tumor Size(>=3cm)	4.3	2.0-9.1	0.001
LN Metastasis	4.6	2.3-9.3	<0.001
Differentiation (G3.4)	2.7	1.0-6.9	0.047
GPS	5.5	2.6-11.7	<0.001

Table 4. The Results of a Multivariate Survival Analysis Examining the Association between the Glasgow Prognostic Scores (GPS) and Survival

Palameter	HR	95% CI	p value
Gender	1.6	0.6-4.7	0.372
Smoking	3.1	1.1-9.1	0.04
Tumor Size(>=3cm)	2.9	1.3-6.7	0.011
LN metastasis	2.0	0.9-4.5	0.904
Differentiation (G3.4)	0.6	0.1-4.4	0.63
GPS	2.9	1.2-6.7	0.013

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Abbreviation
GPS: Glasgow Prognostic Score
CRP: C-reactive protein
NSCLC: non-small cell lung cancer
HR: hazard ratio

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