Original article (Clinical Original)

Inflammation-based scoring is a useful prognostic predictor of pulmonary resection for elderly patients with clinical stage I non-small cell lung cancer

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Word count of abstract: 349

Word count of text: 2613

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Abstract

Objectives: The number of elderly lung cancer patients requiring surgery has been increasing due to the aging society and less invasive perioperative procedures. Elderly people usually have various comorbidities, but there are few simple and objective tools that can be used to determine prognostic factors for elderly patients with clinical stage I non-small cell lung cancer (NSCLC). The aim of this retrospective study was to evaluate the prognostic factors of surgically treated, over 80-year-old patients with clinical stage I NSCLC.

Methods: The preoperative data of 97 over 80-year-old patients with clinical stage I NSCLC were collected at Nagasaki University hospital from 1990 to 2012. As prognostic factors, inflammation-based scoring systems, including the Glasgow prognostic score (GPS) determined by serum levels of C-reactive protein and albumin, the neutrophil lymphocyte ratio (NLR), and the platelet lymphocyte ratio (PLR), were evaluated, as well as other clinicopathological factors, including performance status, body mass index, carcinoembryonic antigen, Charlson comorbidity index, and type of surgical procedure.

Results: The median age was 82 (range, 80-93) years. There were 62 (64.0%) clinical stage IA cases and 35 IB cases. Operations included 64 (66.0%) lobectomies, 15 segmentectomies, and 18 wedge resections. The pathological stage was I in 76 (78.4 %) patients, II in 12 (12.4%), III in 8 (8.2%), and IV in 1 (1.0%). Twelve (12.4%) patients underwent mediastinal lymph node dissection. Overall survival and disease-specific 5-year survival were 55.5% and 70.0%, respectively. The average GPS score was 0.4 (0-2). Disease-specific 5-year survival was significantly longer with GPS 0 than with GPS 1-2. (74.2%, 53.7%, respectively, p=0.03). Overall 5-year survival was significantly longer with GPS 0 that with GPS 1-2. (59.7%, 43.1%, respectively, p=0.005). Both the NLR (median value = 1.9) and the PLR (median value = 117) were not correlated with disease-specific and overall 5-year survivals. On multivariate analysis, pathological stage I (p=0.01) and GPS 0 (p= 0.04, hazard ratio: 2.13, 95% confidence interval 1.036-4.393) were significant prognostic factors.

Conclusions: The preoperative GPS appears to be a useful predictor of overall survival and could be a simple prognostic tool for elderly patients with clinical stage I NSCLC.

Key Words: lung cancer, octogenarians, surgery, Glasgow prognostic score.

Introduction

The average age of the population is increasing in most countries including Japan, which has already become one of the world's fastest aging countries. According to the 2013 statistical analysis of the Japanese Health and Welfare Ministry, life expectancy was 8.6 years for men and 11.5 years for women in their 80s [1]. In addition, non-small cell lung cancer (NSCLC) remains one of the commonest causes of cancer deaths worldwide. Recently, several reports have shown that surgery for lung cancer in elderly people, including octogenarians, is a safe and feasible treatment [2-6] even for nonagenarians [7]. However, surgeons are sometimes reluctant to perform pulmonary resections because the surgical mortality and morbidities in elderly people are expected to be higher than in younger patients, and the life expectancy of elderly people with lung cancer could be limited by death from natural causes [2]. Radiotherapy also yields similar results for early-stage lung cancer [8]. Therefore, careful attention has to be paid when deciding the surgical treatment strategy for elderly persons. To solve this problem, there have been several reports about prognostic factors for overall survival and for postoperative complications [3-5, 9]. Endo et al [5] reported that elderly lung cancer patients with a Charlson comorbidity index [9] (CCI) $\geq$2 had poorer survival. Recently, inflammation-based scores have been reported as simple, useful, and objective prognostic predictors for cancer patients [10-13]. For example, Leung et al [14] reported that the pretreatment Glasgow prognostic score (GPS) was an important predictor of cancer-specific survival in patients with inoperable NSCLC. However, these reports were intended for advanced stage patients needing chemotherapy [15], not for early-stage patients, such as resectable lung cancer patients. The purpose of this retrospective study was to identify the prognostic factors for overall survival of elderly patients (80 years and over) with clinical stage I NSCLC

Patients and methods

Patients

Between 1990 and 2012, 97 patients aged 80 years and over with clinical stage I NSCLC underwent pulmonary resection at Nagasaki University Hospital. Patients' age, sex, performance status (Eastern cooperative oncology group: PS), body mass index (BMI), serum carcinoembryonic antigen (CEA), CCI, clinical and pathological status, and the type of pulmonary resection and lymph node dissection were examined. Three inflammation-based scores, the GPS, the neutrophil lymphocyte ratio (NLR), and the platelet lymphocyte ratio (PLR), were also evaluated. Preoperative staging routinely included chest X-rays, chest computed tomography (CT), magnetic resonance imaging (MRI) of the brain, and positron emission tomography (PET)/CT scan. Clinical N0 was radiographically confirmed by lymph nodes with a short axis of less than 1 cm on chest CT and no accumulation of fluorodeoxyglucose on PET/CT. Bone scintigraphy and abdominal CT were used until PET/CT could be routinely used. A complete evaluation of cardiac and respiratory functions was performed to ensure that patients could tolerate pulmonary resection. The extent of pulmonary resection and systemic mediastinal or hilar lymph node dissection was determined according to clinical stage, PS, and comorbidity.

Measurement of inflammation-based scores

Glasgow Prognostic Score (GPS), Neutrophil Lymphocyte Ratio (NLR), and Platelet Lymphocyte Ratio (PLR)

The GPS was determined as previously described [10]. The GPS consists of two parameters, C-reactive protein (CRP) and albumin. Patients with both elevated CRP (>1.0 mg/dL) and hypoalbuminemia (<3.5 mg/dL) were allocated a score of 2. Patients with only one of these biochemical abnormalities were allocated a score of 1. Patients with neither of these abnormalities were allocated a score of 0. The NLR and PLR were calculated as the ratios of the neutrophils and platelets to lymphocytes; their median values were used because their distributions were not normal. The patients were separated into two groups according to the median values of NLR and PLR, and disease-specific and overall survivals were compared. These inflammation-based scores were based on

preoperative data. In this study, no patients showed obvious infection or other inflammatory states, such as obstructive pneumonia and atelectasis.

Statistical Analysis

The relationships among GPS groups were examined using the Kruskal-Wallis test. Disease-specific and overall survivals were analysed using the Kaplan-Meier method and the log-rank test. Multivariate survival analysis was performed with a Cox proportional hazard regression model. *P* values less than 0.05 were considered significant. JMP® 10 (SAS Institute Inc., Cary, NC, USA) was used for all statistical analyses.

Results

Characteristics of patients and their surgical results

All 97 patients (62 men, 35 women; median age 82 years) underwent pulmonary resection for clinical stage I (IA: 62 and B: 35 patients) NSCLC. The preoperative comorbidities of the patients included chronic pulmonary disease (35 case, 36.1%), coronary artery disease (19 cases, 19.9%), any prior tumour within 5 years (13 cases, 13.4%), diabetes mellitus (10 cases, 10.3%), and so on. These comorbidities are shown in Table 1. The surgical procedures included 64 (66.0%) cases of lobectomy, 15 (15.5%) cases of segmentectomy, and 18 (18.6%) cases of wedge resection. Twelve (12.4%) patients underwent mediastinal lymph node dissection. The pathological stage was I in 76 (78.4 %) patients, II in 12 (12.4%), III in 8 (8.2%), and IV in 1 (1.0%). No patients died within 30 days of surgery. The postoperative comorbidities consisted of atrial fibrillation (9 cases, 9.8%), prolonged (≥7 days) air leakage (8 cases, 8.2%), pneumonia (7 cases, 7.2%), and so on, all of which were successfully treated. Disease-specific and overall 5-year survivals were 70.0% and 55.0%, respectively (Fig.1). Twenty-one (21.7%) cases died due to recurrence of lung cancer, and 15 (15.7%) cases died

due to other causes, including 3 of pneumonia, 2 of heart failure and fatal arrhythmia, 1 each of interstitial pneumonia, cerebral infarction, rectal cancer, panperitonitis, and an accident, while 3 died of unknown causes.

Analysis of prognostic factors

Table 2 shows the characteristics and 5-year survival rates according to potential prognostic factors in the clinical stage I elderly people of this study. Four major prognostic factors, including patient factors (sex, PS, BMI, serum CEA, and CCI), inflammation factors (GPS, NLR, and PLR), surgical factors (procedures and lymph node dissection), and stage factors (clinical and pathological), were investigated.

Patient factors

PS, BMI, and serum CEA value were not significant, but sex was marginally significant (p=0.05). For CCI, the average score was 1.3 (range: 0-5). Disease-specific 5-year survival was not significantly different between CCI 0,1 and CCI ≥2 (71.6%, 64.4%, respectively, p=0.48) (Fig.2A), but overall 5-year survival was significantly longer for CCI 0,1 than for CCI ≥2 (63.2%, 36.5%, respectively, p=0.03) (Fig 2B).

Inflammatory factors

The average GPS score was 0.4 (range: 0-2). Disease-specific 5-year survival was significantly longer with GPS 0 that with GPS 1-2 (74.1%, 53.7%, respectively, p=0.03) (Fig.3A). Overall 5-year survival was significantly longer with GPS 0 than with GPS 1-2 (59.7%, 43.1%, respectively, p=0.005) (Fig.3B). Table 3 shows the patients' characteristics according to GPS. The patients' background characteristics, including patient, inflammatory, surgical, and stage factors, except for the distribution of PLR, were not significantly different among GPS 0, 1, and 2. The median NLR value was 1.9 (range: 0.3-7.5). Disease-specific and overall 5-year survivals were not significantly different

between NLR ≥2 and NLR <2 (p= 0.15, p=0.57, respectively). The median PLR value was 117 (range: 48-369). Disease-specific and overall 5-year survivals were not significantly different between PLR ≥118 and PLR<118 (p= 0.66, p=0.34, respectively).

Surgical and Stage Factors

Surgical procedures (lobectomy / limited, i.e. segmentectomy and wedge resection) and lymph node dissection (mediastinal / limited) were not identified as significant prognostic factors (p=0.11, p=0.92, respectively). Clinical stage (IA / IB, i.e. tumour size) was also not identified as a significant prognostic factor. However, 5-year survival was significantly different between pathological stage I and stages II, III, and IV (64.7%, 27.3%, p<0.01)

Multivariate analysis of overall survival in elderly people with clinical stage I showed that pathological stage I (p=0.01, hazard ratio: 2.48, 95% confidence interval) and GPS 0 (p= 0.04, hazard ratio: 2.13, 95% confidence interval 1.036-4.393) were significant prognostic factors for a good outcome (Table 4).

Discussion

This retrospective analysis based on individual data of 97 elderly patients who underwent pulmonary resection for clinical stage I NSCLC demonstrated that preoperative GPS was a significant prognostic factor, as well as pathological stage, which is well known as the most important prognostic factor.

Many countries have been rapidly progressing to become aging societies, and NSCLC still remains one of the commonest causes of cancer deaths worldwide. Thus, the number of elderly patients with potentially resectable lung cancer will be increasing. On the other hand, aging results in physiological deterioration in the respiratory, cardiovascular, and renal systems, and other major organs. In the present study, 36% of elderly patients had chronic pulmonary disease, and 20% had coronary artery disease according to CCI. In addition, more surgical comorbidities are seen in elderly patients than in

younger patients [16]. Surgeons will have to face the difficult problem of whether to perform surgery for such elderly patients with several comorbidities.

Recently, inflammation-based scores, including the GPS, the NLR, and the PLR, have been reported as objective predictors for various cancer patients [10-12], including lung cancer patients [14, 15, 17]. However, these reports were targeted to advanced stage patients, requiring chemotherapy, including patients of various backgrounds. Thus, the present study exclusively investigated the usefulness of these inflammation-based scores for surgically resectable elderly patients with clinical stage I NSCLC. It is increasingly recognized that the host systemic inflammatory response plays a critical role in the development and progression of many cancers [10-15, 17, 18]. The detailed mechanism and significance of inflammatory response have been fully described elsewhere [10-15, 17, 18]. In brief, cancer growth and eventual invasion produce local tissue damage, which disrupts homeostasis and incites systemic acute-phase responses [13]. Simultaneously, the progression of cancer releases proinflammatory cytokine (i.e. Interleukin 6) and promotes the immunovascular system (neutrophils and lymphocytes), and CRP, albumin, neutrophil, platelet and lymphocyte are affected and have been used as good ongoing systemic inflammatory response markers in clinical practice.

McMillan [12] et al reviewed the GPS and reported that it was the most extensively validated of the systemic inflammation-based prognostic scores in a variety of clinical scenarios, such as operable disease, chemo/radiotherapy, inoperable disease, and even in unselected cohorts. In addition, an increased GPS was associated with increased weight and muscle loss, poor PS, increased comorbidity, increased pro-inflammatory and angiogenic cytokines, and complications with treatment. In the present study, there were no significant differences in background characteristics, BMI, PS and clinical and pathological stage among GPS 0, 1, and 2 (Table 3). However, the number of GPS 2 was so limited (7 cases) that more cases are needed to whether high GPS is correlated with such parameters. On the other hand, the present results showed that disease-specific 5-year survival was significantly longer with GPS 0 than with GPS 1-2 (74.1%, 53.7%, respectively, $p=0.03$). Overall 5-year survival was significantly longer with GPS 0 than with GPS 1-2 (59.7%, 43.1%, respectively, $p=0.005$).

Moreover, on multivariate analysis, GPS appeared to be a significant prognostic factor for overall survival, even in elderly patients with clinical stage I NSCLC, which seems to have less of an inflammatory component than the advanced stage. In fact, though the cases were limited, the 5-year survival of GPS 0 (18 cases) and GPS 1-2 (5 cases) in advanced stage (stage II, III and IV) of elderly patients were not significant during the same period of this research.

NLR and PLR have also been reported as prognostic factors [11, 17, 18], and Templeton [18] and Zhou [11] et al reviewed the prognostic value of NLR and PLR in various cancers and reported that elevated NLR and PLR levels were negative predictors for overall survival in patients with NSCLC (hazard ratio=1.66 and 1.85, respectively). Two reasons may explain why NLR and PLR were not identified as prognostic factors in the present study.

First, median values were used as cut-off values for NLR and PLR. However, the NLR and GPS have remained controversial because their cut-off values could not be defined consistently. For the NLR, according to a meta-analysis of 100 studies [18], the cut-off for high NLR was 4.0 (range = 1.9-7.2). In the present study, NLR>4 could not be used because only 5 (5.2%) of 97 patients had NLR>4. This was not appropriate for statistical analysis. For the PLR, according to a meta-analysis of 26 studies [11], the cut-off values ranged from 100 to 300 in 26 studies (9 of 26 studies cut-off <160, 10 studies cut-off ≥160, and the remaining 7 had triple subsets of PLR cut-offs, with six using 150/300 and one using 100/200). The definition of cut-off values might affect the present results, while the GPS was different in that it was categorized using only 3 points (0, 1, and 2). We would recommend using the GPS more than the NLR and PLR as inflammation-based scores for clinical stage I NSCLC. Second, this retrospective study involved elderly patients with clinical stage I NSCLC, which is regarded as an early stage of cancer. Thus, a significant effect of systemic inflammation might not be identified by NLR and PLR.

Other factors including patients' factors (PS, BMI, and serum CEA), surgical factors (procedures and lymph node dissection), and clinical stage were not identified as significant prognostic factors, except for sex (marginally significant p=0.05). We should accept these results, especially surgical factors, because we have previously reported [19] that there was no significant difference in the

overall survival and local recurrence rates between the with and without lymph node dissection groups for elderly patients with clinical stage I NSCLC and concluded that a limited operation without lymph node dissection might be the best surgical treatment for carefully selected elderly patients with clinical stage I NSCLC.

In addition, the small sample size of the present study might affect other typical prognostic factors, PS and CEA [20]. From the results of the present study, we suggest the following for determining the appropriateness of surgery for elderly patients with clinical stage I NSCLC. Surgical candidates basically require a good performance status and preserved respiratory and cardiac functions for procedures, and a low score GPS is desirable. Radical pulmonary resection is not always necessary, and VATS is the best approach [21] because it is less invasive [22] and less painful [23]. On the other hand, a patient with GPS ≥2 might benefit less from surgery. Thus, high GPS would change our clinical practice in regards to management of elderly lung cancer patients.

This study had several limitations. First, this study was retrospective, and the sample population was small and median follow-up of only 2.8 years and obtained from a single institution; small samples and short time of follow-up sometimes affect statistical accuracy. Secondly, since cut-off values of NLR and PLR have not been defined, they might not have been identified as prognostic factors. Thirdly, the long period of time examined (23years) during which many diagnostic and technical advances, such as PET/ CT, VATS and postoperative intensive care evolved. This long period of time would be another selection bias. Thus, we should have limited the analysis to a short time during which all the patient management had been homogenous. Future studies are needed to address these limitations and to determine whether this inflammation-base score could be applied in clinical practice to help determine the appropriateness of surgery for elderly or younger patients, or advanced stage with NSCLC.

In conclusion, to the best of our knowledge, this is the first study to evaluate the prognosis of elderly patients with operable clinical stage I NSCLC using the preoperative GPS. The preoperative GPS should be used routinely in clinical practice, since it appears to be a useful predictor of overall survival and could be a simple, versatile, and objective prognostic tool for elderly patients with

clinical stage I NSCLC.

Funding

None

Acknowledgments

None

Conflict of interest: none declared

Table 1. Preoperative comorbidities of elderly patients

Comorbidity	Number of patients	%
Chronic pulmonary disease	35	36.1
Coronary artery disease	19	19.9
Any prior tumour within 5 years	13	13.4
Diabetes mellitus	10	10.3
Cerebrovascular disease	6	6.2
Peripheral vascular disease	5	5.2
Moderate to severe renal disease	5	5.2
Congestive heart failure	3	3.1
Connective tissue disease	3	3.1
Peptic ulcer disease	2	2.1
Dementia	2	2.1

Table 2. 5-year survival rates according to potential prognostic factors in clinical stage I elderly patients with NSCLC

Factors	Variable	Number of patients	5-year survival (%)	p value
Patient Factors	Sex (male / female)	62 / 35	43.3 / 71.7	0.05
	Performance Status (0 / 1, 2)	58 / 39	70.5 / 47.7	0.06
	Body Mass Index (< 22 / ≥22 kg/m^2)	46 / 51	53.5 / 56.5	0.84
	CEA (≤5 / >5)	65 / 32	49.8 / 62.2	0.89
	CCI (0,1 / ≥2)	64 / 33		
	Overall		63.2 / 36.5	< 0.05
	Disease-Specific		71.6 / 64.4	0.48
Inflammatory Factors	GPS (0 / 1, 2)			
	Disease-Specific	65 / 32	74.1 / 53.7	< 0.05
	Overall		59.7 / 43.1	< 0.01
	NLR (< 2 / ≥2)			
	Disease-Specific	54 / 43	64.9 / 80.1	0.15
	Overall		49.7 / 68.2	0.57
	PLR			

	(< 118 / ≥118)			
	Disease-Specific	49 / 48	73.4 / 66.8	0.66
	Overall		51.8 / 60.7	0.34
Surgical Factors	Surgical procedure (Lobectomy / Limited)	64 / 33	59.6 / 41.2	0.11
	Lymph node dissection (ND2 / Limited)	21 / 76	54.9 / 56.5	0.92
Stage Factors	Clinical Stage (IA / IB)	62 / 35	50.4 / 58.2	0.67
	Pathological Stage (I / II, III, IV)	76 / 21	64.7 / 27.3	< 0.01

CEA: Carcinoembryonic antigen

CCI: Charlson Comorbidity Index

GPS: Glasgow Prognostic Scale

NLR: Neutrophil Lymphocyte Ratio

PLR: Platelet Lymphocyte Ratio

ND: Nodal dissection

Table 3. Patient characteristics according to the Glasgow Prognostic Score

		GPS 0	GPS 1	GPS 2	p value
Number (%)	Patients	65 (67.0)	25 (25.8)	7 (7.2)	
Patient Factor	Age (median)	82	82	83	0.41
	Sex				
	Male	40 (61.5)	15 (60.0)	7 (100)	0.12
	Female	25 (38.5)	10 (40.0)	0 (0)	
	Performance Status				
	0	42 (64.6)	11 (44.0)	5 (71.4)	0.24
	1	20 (30.1)	14 (56.0)	2 (28.6)	
	2	3 (4.6)	0 (0)	0 (0)	
	Body Mass Index				
	≤22 kg/m^2	31 (47.7)	10 (40.0)	5 (71.4)	0.57
	>22 kg/m^2	34 (52.3)	15 (60.0)	2 (28.6)	
	Respiratory function				
	$FEV_{1.0}$ (ml: average)	1904	1761	1859	0.52
	%DLCO (%: average)	92	81	100	0.10
	CEA				
	<5	21 (32.3)	9 (36.0)	2 (28.6)	0.37
	≥5	44 (67.7)	16 (64.0)	5 (71.4)	
	CCI				
	0	19 (29.2)	7 (28.0)	0 (0)	0.17
	1	25 (38.7)	10 (40.0)	3 (42.9)	

	≥2	21 (32.3)	8 (32.0)	4 (57.1)	
Inflammatory Factor	NLR				
	<2	34 (52.3)	17 (68.0)	3 (42.9)	0.17
	≥2	31 (47.7)	8 (32.0)	4 (57.1)	
	PLR				
	< 118	27 (41.5)	18 (72.0)	4 (57.1)	0.04
	≥118	38 (58.5)	7 (28.0)	3 (42.9)	
Surgical Factor	Surgical procedure				
	Lobectomy	47 (72.3)	15 (60.0)	2 (28.6)	0.05
	Limited	18 (27.7)	10 (40.0)	5 (71.4)	
	Lymph node dissection				
	ND2	15 (23.1)	5 (20.0)	1 (14.3)	0.84
	Limited	50 (76.9)	20 (80.0)	6 (85.7)	
Stage Factor	Clinical Stage				
	IA	46 (70.8)	12 (48.0)	4 (57.1)	0.12
	IB	19 (29.2)	13 (52.0)	3 (42.9)	
	Pathological Stage				
	I	54 (83.1)	17 (68.0)	5 (71.4)	0.23
	II	7 (10.8)	4 (16.0)	1 (14.3)	
	III	4 (6.1)	3 (12.0)	1 (14.3)	

IV	0	1 (4.0)	0

GPS: Glasgow Prognostic Scale

$FEV_{1.0}$: Forced expiratory volume in one second

%DLCO: %diffusing capacity for carbon monoxide

CEA: Carcinoembryonic antigen

CCI: Charlson Comorbidity Index

NLR: Neutrophil Lymphocyte Ratio

PLR: Platelet Lymphocyte Ratio

ND: Nodal dissection

Table 4. Multivariate analysis of survival in clinical stage I elderly people: Cox proportional hazard model

Factors	Variable	Reference	Hazard Ratio	95% CI	p value
Patient Factors	Sex (male)	female	1.57	0.661 - 3.716	0.31
Inflammatory Factors	CCI (2-)	0, 1	1.60	0.578 - 4.395	0.34
	GPS (1, 2)	0	2.13	1.036 - 4.393	0.04
Stage Factors	p-Stage (II, III, IV)	I	2.48	1.211 - 5.076	0.01

CCI: Charlson Comorbidity Index

GPS: Glasgow Prognostic Scale

CI: Confidence Interval

Figure legends

Fig. 1. Disease-specific and overall survival curves in elderly clinical stage I lung cancer patients. Disease-specific and overall 5-year survivals are 70.0% and 55.5%, respectively.

Fig. 2. Comparisons of disease-specific survival curves (A) and overall survival curves (B) between Charlson comorbidity index (CCI) 0,1 (n=64) and CCI ≥2 (n=33). Disease-specific 5-year survival is not significantly different between CCI 0,1 and ≥CCI 2 (71.6%, 64.4%, respectively, p=0.48). Overall 5-year survival is significantly longer with CCI 0,1 than with CCI ≥2(63.2%, 36.5%, respectively, p=0.03)

Fig. 3. Comparisons of disease-specific survival curves (A) and overall survival curves (B) between Glasgow prognostic score (GPS) 0 (n=65) and GPS 1+2 (n=32). Both 5-year survival rates are significantly different ($p < 0.05$ and $p<0.01$) between the two groups.

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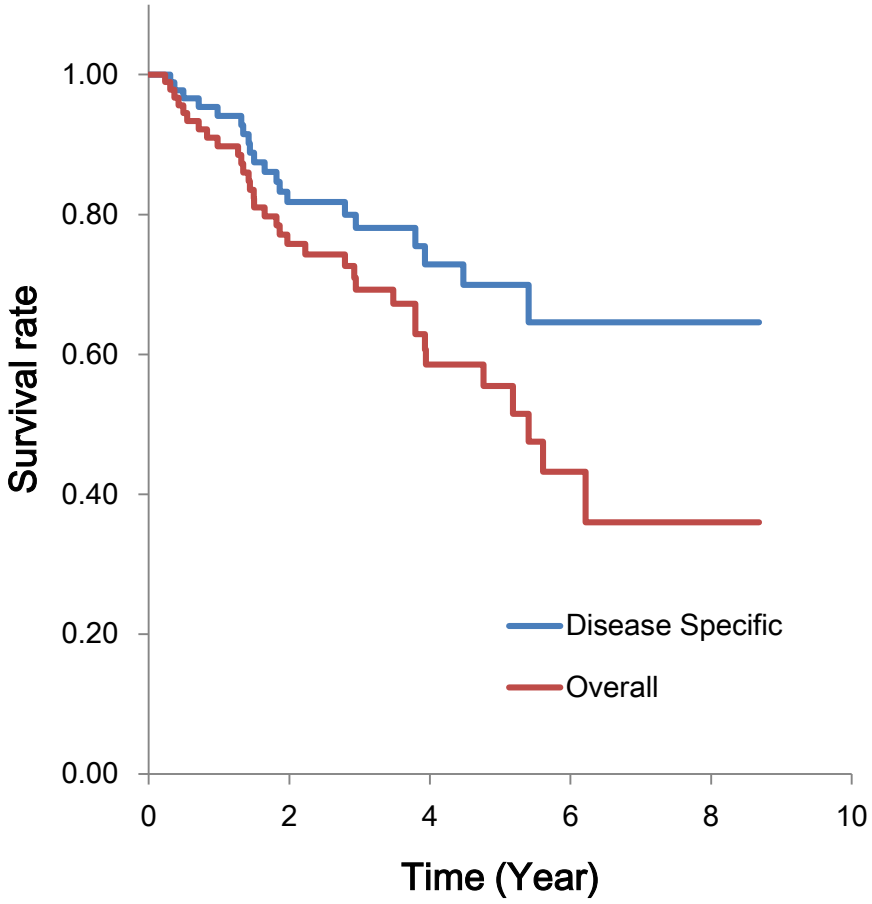
1.00
0.80
0.60
0.40
0.20
0.00
Survival rate
0
2
4
6
8
10
Time (Year)
Disease Specific
Overall

Figure 1

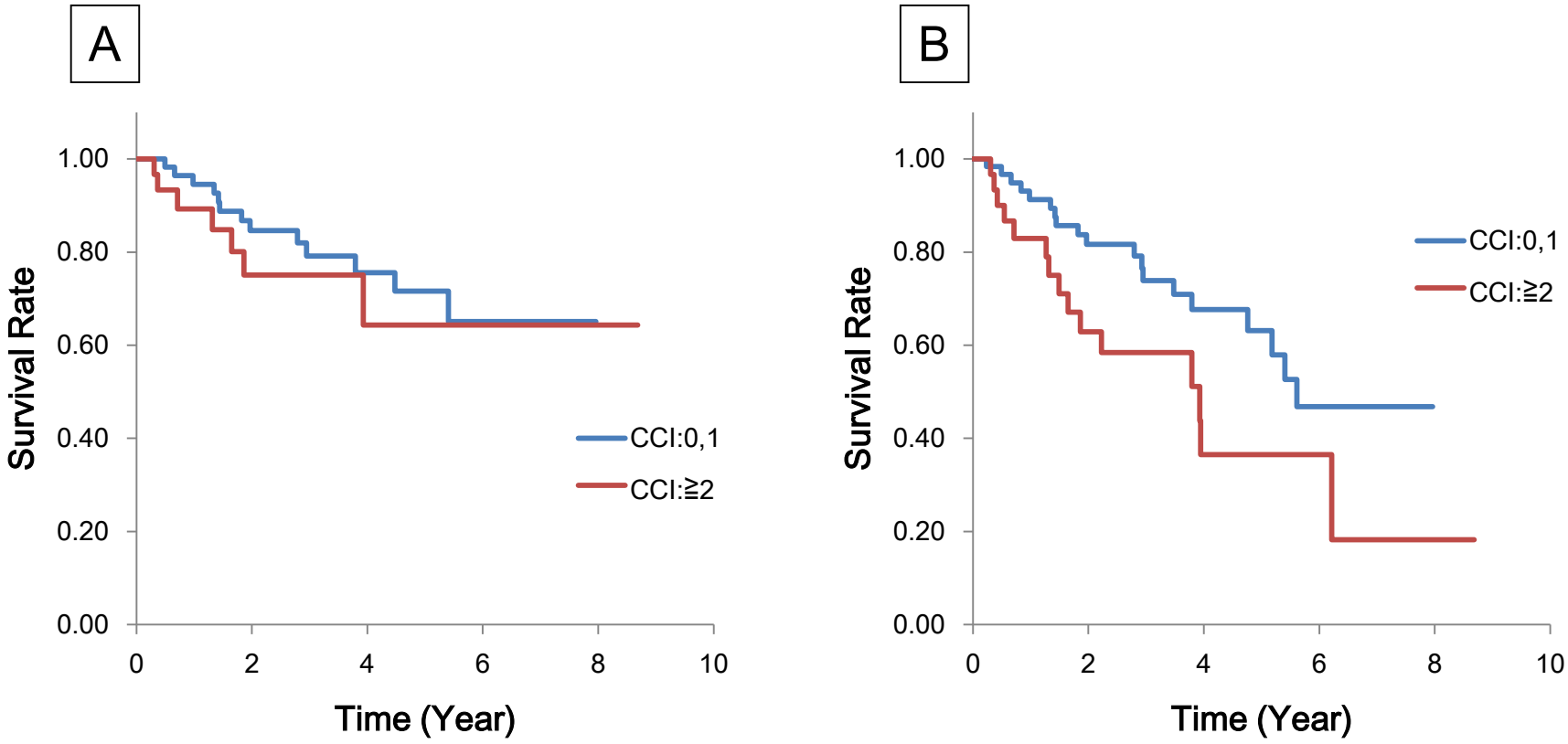
A
1.00
0.80
0.60
0.40
0.20
0.00
Survival Rate
0
2
4
6
8
10
Time (Year)
CCI:0,1
CCI:≧2
B
1.00
0.80
0.60
0.40
0.20
0.00
Survival Rate
0
2
4
6
8
10
Time (Year)
CCI:0,1
CCI:≧2

Figure 2

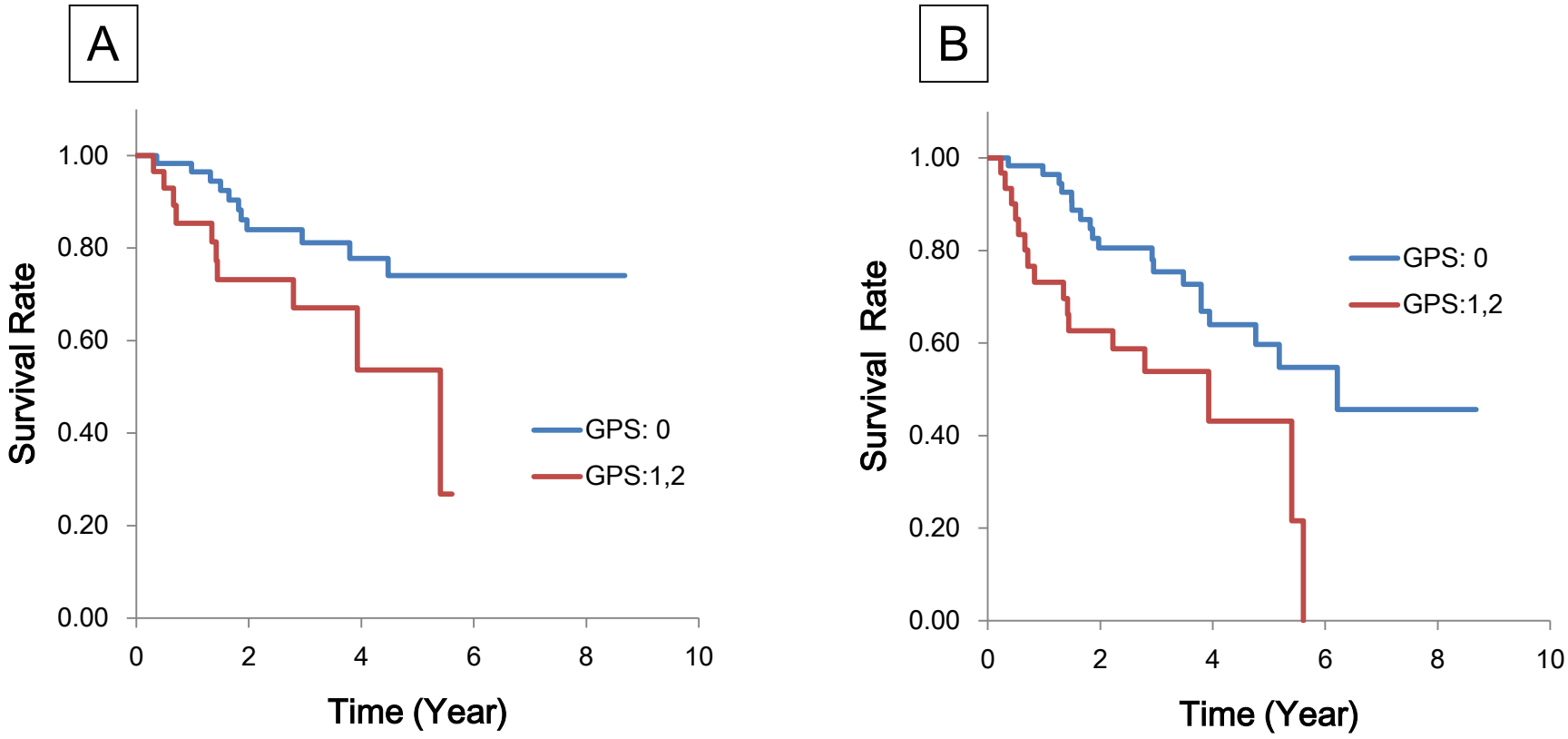
A
1.00
0.80
0.60
0.40
0.20
0.00
Survival Rate
0
2
4
6
8
10
Time (Year)
GPS: 0
GPS:1,2
B
1.00
0.80
0.60
0.40
0.20
0.00
Survival Rate
0
2
4
6
8
10
Time (Year)
GPS: 0
GPS:1,2

Figure 3