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Comparison of Charlson comorbidity index and Kaplan—Feinstein index in patients with stage I lung cancer after surgical resection

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Abstract

Objective: We sought to determine whether Charlson comorbidity index (CCI) or Kaplan—Feinstein index (KFI) is a better predictor of prognosis in patients with stage I NSCLC after surgical resection. **Methods:** A retrospective study of medical records of 426 patients with stage I lung cancer having complete surgical resection from 1995 to 2000 was performed. Data collected included age, gender, smoking history, resection type, pleural invasion status, and tumor type and size. Comorbidity score was determined using Charlson comorbidity index and Kaplan—Feinstein index. Both univariate and multivariate analyses were used to evaluate prognostic factors. **Results:** Three hundred and twenty-eight male (76.99%) and 98 female (23.01%) patients had a mean age of 67.07 years (range 19—88 years). Median duration of follow-up was 60.32 months. Total follow-up rate was 95.1%. Distribution of CCI score was: 0, 236 (55.40%); 1, 112 (26.29%); ≥2, 78 (18.31%). Overall KFI score was: none, 247 (57.98%); mild, 126 (29.58%); moderate, 43 (10.09%); and severe, 10 (2.35%). In univariate analyses, patients aged ≥65 years, male, smokers, CCI score ≥2, extensive resection and pathological stage IB cancer had poorer 5-year survival. In multivariate logistic regression analysis, age ≥65 years, pneumonectomy, CCI score ≥2, and stage IB cancer were independent prognostic factors for poorer 5-year survival. **Conclusions:** Patients with CCI ≥2 had higher perioperative mortality and death from non-cancer causes after surgery compared to patients with CCI <2. However, KFI score had no impact on operative mortality and non-cancer death during follow-up.

Keywords: Comorbidity; Charlson score; Kaplan—Feinstein index; Lung cancer; Survival analysis

1. Introduction

Lung cancer remains the leading cause of cancer death in most countries. Although multimodality treatment has been advocated, the prognosis is still poor. For patients with stage I non-small cell lung cancer (NSCLC), surgical resection is a potentially curable therapy and provides satisfactory results [1]. According to the new TMN staging system revised in 1997, stage I is divided into stage IA (T1N0M0) and IB (T2N0M0) [2]. Although complete surgical resection can be achieved in most patients with stage I cancer, prognosis differs significantly for patients with stage IA and stage IB cancer. The 5-year survival rate in patients with stage IA cancer is 66—80%, while in patients with stage IB cancer, the 5-year survival rate is only 35—65% [1—4]. Presence of symptoms, weight loss, and poor performance status at the time of diagnosis have been found to have a significant negative impact on survival in patients with stage I NSCLC [5,6]. Comorbidity can be an important predictor of survival in patients with a variety of neoplasms [7—12]. Among the methods of comorbidity measurement, Charlson comorbidity index (CCI) is the most widely used till date [13]. Birim et al. reported that the Charlson comorbidity index is a better predictor of survival than individual comorbid conditions in lung cancer surgery [14]. The Kaplan—Feinstein index (KFI) was developed in 1974 and had been used as a predictor of survival in some types of cancer [7,8,15,16]. Battafarano et al. reported the impact of comorbidity on survival in patients with stage I NSCLC using the KFI [16]. The authors concluded that comorbidity has a significant impact on survival after surgical resection of patients with stage I NSCLC. Firat et al. also studied the significance of comorbidity and Karnofsky performance scores in stage I NSCLC patients and found that cumulative illness rating scale for geriatrics (CIRS-G) score of 65 and

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KPS < 70 indicate a poorer prognosis in patients with stage I NSCLC [17]. Little research has examined which comorbidity rating best evaluates the impact on survival of patients with NSCLC. In this study, we aim to determine whether CCI or KFI is a better predictor of prognosis in patients with stage I NSCLC after surgical resection.

2. Materials and methods

2.1. Population under study

A retrospective study was performed of medical records of 426 patients with stage I lung cancer having complete surgical resection from 1995 to 2000 at Taipei Veteran General Hospital, Taipei, Taiwan. Patients with previous treatment for lung cancer and preoperative chemo-irradiation were excluded. Data collected by chart review included age, gender, smoking history, type of resection, pleural invasion, tumor type, and tumor size. Comorbidity score was determined using two scoring systems, CCI and KFI. Patients were followed for 1 month after surgery and then every 3 months for the first 2 years, every 6 months for the next 3 years, and every year thereafter. Zero time was the date of pulmonary resection, and the terminal event was the end of this study – patient's death, or the last contact date of patients lost to follow-up.

2.2. Comorbidity severity

The CCI takes into account both the number and seriousness of comorbid diseases. Components of the weighted index are shown in Table 1 [13]. The index is divided into three groups: 0, 1, and ≥2. KFI classifies the pathophysiologic derangement of each comorbid ailment according to a four-category system: 0, 1, 2, and 3. An overall comorbidity score is determined on the basis of the number of ailments and their individual degrees of severity. The organ systems examined in the modified KFI are outlined in Table 2 [15].

Table 1
Charlson comorbidity index (CCI) scoring

Assigned weight for disease	Conditions
1	Myocardial infarct Congestive heart failure Peripheral vascular disease Cerebrovascular disease Dementia Chronic pulmonary disease Connective tissue disease Ulcer disease Mild liver disease Diabetes
2	Hemiplegia Moderate or severe renal disease Diabetes with end-organ damage Any tumor Leukemia Lymphoma
3	Moderate or severe liver disease
6	Metastatic solid tumor AIDS

Assigned weight for each patient's condition. The total equals the score. Example: chronic pulmonary (1) and lymphoma (2) = total score (3).

2.3. Statistical analysis

Descriptive statistics were used to describe the patients' characteristics and outcomes. Normally distributed continuous data are expressed as mean ± standard deviation (SD) throughout. Medians with ranges are used when continuous data are not normally distributed. Categorical data are expressed as counts and proportions. The chi-square test or Fisher's exact test were used to assess the differences between variables in independent groups. Survival analysis was performed using the Kaplan–Meier method, and survival differences were tested using the log-rank test. Variables for which $p < 0.1$ in univariate analysis were put into the multivariate analysis. All data analysis was performed with Systat 14.0 for Windows (SPSS Inc., Chicago, IL) and $p < 0.05$ was considered significant.

Table 2
Organ system examined in the modified Kaplan–Feinstein index (KFI)

Cardiovascular system
Myocardial infarction
Angina or coronary artery disease
Congestive heart failure
Arrhythmia
Hypertension
Venous disease
Peripheral arterial disease
Respiratory system
Restrictive lung disease
Chronic obstruction pulmonary disease
Gastrointestinal system
Hepatic disease
Stomach or intestinal disease
Pancreatic disease
Renal system
End-stage renal disease
Endocrine system
Diabetes mellitus
Neurologic system
Stroke or cerebrovascular accident
Dementia
Paralysis
Neuromuscular disease
Psychiatric system
Rheumatologic system
Immunologic system
AIDS
Malignancy
Solid tumor
Leukemia and myeloma
Lymphoma
Substance abuse
Alcohol
Illicit drug
Body weight or obesity

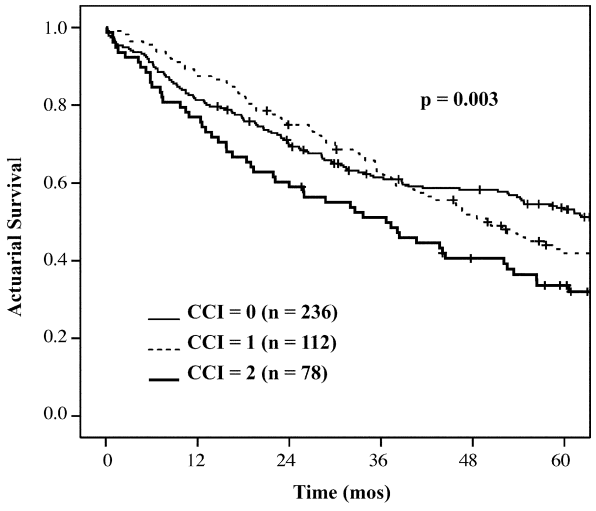
3. Results

The demographic characteristics and 5-year survival of these 426 patients with stage I lung cancer are shown in Table 3. Three hundred and twenty-eight (76.99%) patients were male and 98 (23.01%) patients were female with the mean age of 67.07 years (ranging from 19 to 88 years). Median duration of follow-up was 60.32 months. Twenty-one patients were lost to follow-up. Total follow-up rate was 95.1%. The distribution of CCI score was as follows: 0, 236 (55.40%); 1, 112 (26.29%); ≥2, 78 (18.31%). Overall KFI score was as follows: none, 247 (57.98%); mild, 126 (29.58%); moderate, 43 (10.09%); and severe, 10 (2.35%). Overall operative mortality was encountered in 14 patients (3.3%). In univariate analyses, patients aged ≥65 years, male, smokers, with CCI score ≥2, extensive resection and pathological stage IB cancer had poorer 5-year survival. Tumor type, pleural invasion, and KFI were non-significant prognostic factors.

Table 3
Results of univariate analysis and 5-year survival rate of 426 patients with stage I lung cancer

Variables	Number (%)	5-year survival (%)	*p*-value[a]
Total	426		
Age (years, mean age ± SD)	67.07 ± 10.27		
Age (years)			
<65	123 (28.87)	62.6	0.002
≥65	303 (71.13)	49.8	
Gender			
Male	328 (76.99)	49.5	0.016
Female	98 (23.01)	63.2	
Smoking status			
Smoker	281 (65.96)	50.1	0.023
Nonsmoker	145 (34.04)	60.0	
Charlson comorbidity index grade			
0	236 (55.40)	59.3	0.003
1	112 (26.29)	50.6	
≥2	78 (18.31)	39.7	
Kaplan–Feinstein index			
0	247 (57.98)	57.8	0.126
1	126 (29.58)	45.2	
2	43 (10.09)	55.8	
3	10 (2.35)	40.0	
Type of resection			
Lobectomy	333 (78.17)	57.0	0.039
Wedge + segmentectomy	25 (5.87)	44.0	
Bilobectomy	40 (9.39)	47.5	
Pneumonectomy	15 (3.52)	26.7	
Sleeve lobectomy	7 (1.64)	28.6	
Lobectomy + wedge	6 (1.41)	33.3	
Pathological stage			
IA	142 (33.33)	61.7	0.007
IB	284 (66.67)	49.8	
Pleural invasion			
No	297 (69.72)	55.2	0.644
Yes	129 (30.28)	49.5	
Histologic type			
Adenocarcinoma	204 (47.89)	55.8	0.098
Squamous cell carcinoma	148 (34.74)	46.6	
Bronchoalveolar carcinoma	49 (11.50)	63.1	
Others	25 (5.87)	56.0	

[a] Kaplan–Meier method, log-rank test.

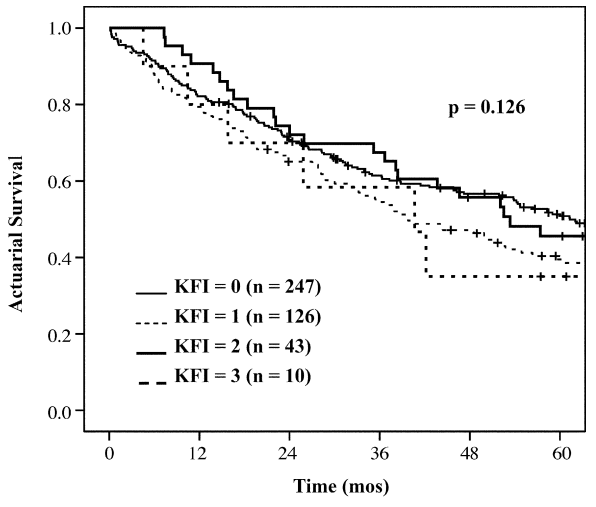


Number of patients at risk

CCI = 0	236	192	161	136	128	113
CCI = 1	112	98	82	68	55	40
CCI = 2	78	60	47	39	29	22

Fig. 1. Five-year survival stratified by Charlson comorbidity index.

Figs. 1 and 2 show the association of comorbidity severity determined according to the CCI and KFI, respectively. In multivariate logistic regression analysis, age ≥65 years, pneumonectomy, CCI score ≥2, and stage IB cancer were



Number of patients at risk

KFI = 0	247	203	171	142	130	111
KFI = 0	126	100	80	67	57	44
KFI = 0	43	39	32	29	22	18
KFI = 0	10	8	7	5	3	2

Fig. 2. Five-year survival stratified by Kaplan–Feinstein index.

Table 4
Results of multivariate analysis of prognostic factors influencing survival

Variables	Hazard ratio	95% CI	*p*-value
Age (years)			
<65	1.000	–	–
≥65	1.402	1.019–1.930	0.038
Sex			
Male	1.000	–	–
Female	0.843	0.566–1.256	0.402
Smoking			
No	1.000	–	–
Yes	1.106	0.773–1.583	0.581
Charlson comorbidity index grade			
0	1.000	–	–
1	1.090	0.804-1.477	0.578
≥2	1.742	1.253–2.423	0.001
Pathological stage			
IA	1.000	–	–
IB	1.492	1.123–1.981	0.006
Type of resection			
Lobectomy	1.000	–	–
Wedge + segmentectomy	1.466	0.875–2.454	0.146
Bilobectomy	1.507	0.950–2.229	0.085
Pneumonectomy	2.419	1.201–3.003	0.011
Sleeve lobectomy	1.856	0.640–4.060	0.312
Lobectomy + wedge	1.986	0.858–5.242	0.103
Histologic type			
Adenocarcinoma	1.000	–	–
Squamous cell carcinoma	1.032	0.762–1.398	0.837
Bronchoalveolar carcinoma	1.019	0.659–1.576	0.931
Others	0.936	0.518–1.693	0.827

95% CI = 95% confidence interval.

independent prognostic factors for poorer survival (Table 4). During the follow-up period, 136 of 426 patients (31.9%) died of recurrent lung cancer, and 95 patients (22.3%) died of other causes. Patients with CCI $\geq$ 2 had higher perioperative mortality and death of non-cancer causes after surgery, compared to patients with CCI $<$ 2 (Table 5; $p = 0.032$ and 0.002, respectively). KFI score had no impact on operative mortality or non-cancer death during the follow-up period in these patients (Table 6).

4. Discussion

Although the prognosis of patients with lung cancer is poor, surgical resection remains the treatment of choice for patients with stage I lung cancer. In general, morbidity after surgical treatment for lung cancer is high because patients with lung cancer are often older and smoke cigarettes. Thus, these patients may be associated with serious comorbidities at the time of diagnosis like atherosclerotic cardiovascular disease, chronic obstructive pulmonary disease, chronic renal insufficiency, and diabetes mellitus. To improve the actual survival of patients with stage I lung cancer after surgery, it is important to understand the impact of comorbidity on their survival. Although several comorbidity measurements have been developed, none have proved to be the standard method to evaluate the prognostic impact on patients with stage I lung cancer after surgery [18]. Birim et al. found CCI strongly correlated with a higher risk of surgery in primary non-small cell lung cancer patients and found it a better predictor than individual risk factors [19]. However, only 144 patients with stage I lung cancer were enrolled in that study and cause of death was not recorded. Moro-Sibilot et al. studied 588 patients with stage I lung cancer having surgical treatment from 1979 to 2003, concluding that CCI was an independent predictor of survival in these patients [20]. However, up to 76 patients (23.2%) in their study died of unknown causes during the follow-up period. In 2005, Colinet et al. designed a new simplified comorbidity score to predict the prognosis of lung cancer patients and concluded that this new simplified comorbidity score is an independent prognostic factor and appears more informative than the CCI in predicting the outcome of lung cancer patients [21]. However, this new scoring system weighted heavily for tobacco consumption, making this scoring system possibly only suitable in evaluating lung cancer patients, not patients with other cancers or disease. In addition, treatment strategies were complex in their patients. Our series focused on the impact of comorbidity on the survival of 426 patients with stage I lung cancer, excluding patients with advanced lung cancer who may need adjuvant chemo-irradiation after surgery. The result demonstrated that CCI is an independent prognostic factor in patients with stage I lung cancer after surgery.

Table 5
Causes of death for 231 patients stratified by preoperative CCI

Preoperative comorbidity	CCI = 0 (*n* = 236) (%)	CCI = 1 (*n* = 112) (%)	CCI ≥ 2 (*n* = 78) (%)	*p*-value[a]
Operative mortality	7 (2.97)	1 (0.89)	6 (7.69)	0.032
Recurrent cancer	76 (32.2)	37 (33.04)	23 (29.49)	0.867
Other	31 (13.14)	27 (24.11)	23 (29.49)	0.002

[a] Pearson chi-square test.

Table 6
Causes of death for 231 patients stratified by preoperative KFI

Preoperative comorbidity	KFI = 0 (*n* = 247) (%)	KFI = 1 (*n* = 126) (%)	KFI = 2 (*n* = 43) (%)	KFI = 3 (*n* = 10) (%)	*p*-value[a]
Operative mortality	8 (3.24)	5 (3.97)	1 (2.33)	0	0.885
Recurrent cancer	79 (31.98)	43 (34.13)	12 (27.91)	2 (20.0)	0.740
Other	39 (15.79)	29 (23.02)	9 (20.93)	4 (40.0)	0.115

[a] Pearson chi-square test.

The Kaplan—Feinstein index has been used in studies of head and neck, breast and lung cancer [7,8,16]. Battafarano et al. reported that KFI comorbidity score had an impact on survival of patients with stage I NSCLC undergoing resection [16]. There was also a trend toward higher perioperative mortality among patients with more severe KFI comorbidity. In contrast, we found in our series that KFI had no influence either on long-term survival or on perioperative mortality in patients with stage I lung cancer after surgery. Instead, we found that CCI score was a prognostic factor in patients with stage I NSCLC after surgical resection, and higher operative mortality rate was also encountered in patients with CCI $\geq$2.

As reported in previous studies, pathological stage and age are also prognostic factors in this study. Besides these factors, comorbidities have an impact on survival of patients with stage I lung cancer and may play a significant role in the treatment plan because patients with serious comorbidities are usually not suitable for adjuvant therapy after surgical resection. After controlling for age, gender, smoking, pathological stage of disease, and type of resection in a multivariate analysis, we found that the risk of death in the follow-up period was significantly higher in patients with CCI $\geq$ 2 than in patients with CCI $<$ 2. The higher risk of death may be attributable to comorbidity, because the proportion of patients with CCI $\geq$ 2 who died of causes other than recurrent cancer is significantly higher than the patients with CCI $<$ 2.

In conclusion, comorbidities are important in evaluating outcome and postoperative care of patients with stage I lung cancer after surgical resection. Stage I lung cancer patients with CCI $\geq$ 2 had higher perioperative mortality and death from non-cancer causes after surgery compared to patients with CCI $<$ 2. KFI score had no impact on operative mortality and non-cancer death during the follow-up period in these patients. To improve survival, efforts should be made to reduce the incidence of recurrent disease with adjuvant treatment and to carefully manage comorbid conditions in these patients.

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