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ORIGINAL RESEARCH

Effect of Insurance Type on Stage at Presentation, Surgical Approach, Tumor Recurrence and Cancer-Specific Survival in Resectable Non-Small Lung Cancer Patients

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Purpose: The aim of this study was to identify the association between Thailand's insurance types and stage at presentation, surgical approach, tumor recurrence and cancer-specific survival in resectable non-small cell lung cancer (NSCLC) patients in northern Thailand.

Patients and Methods: Medical records of patients with NSCLC who underwent pulmonary resection at Chiang Mai University Hospital from January 2007 through December 2015 were retrospectively reviewed. Patients were divided into two groups: patients with the Universal Coverage Scheme (UCS) or Social Security Scheme (SSS) and patients with the Civil Servant Medical Benefit Scheme (CSMBS) or private insurance (PI). Patient characteristics were assessed. The primary outcome was cancer-specific survival while the secondary outcome was tumor recurrence. Cox's regression and matching propensity score analysis was used to analyze data.

Results: This study included 583 patients: 344 with UCS or SSS and 239 with CSMBS or PI. Patients with UCS or SSS were more likely to be active smokers, have a lower percent predicted FEV1, present with higher-stage tumors and worse differentiated tumors, present with tumor necrosis, and undergo an open surgical approach than those with CSMBS or PI. At multivariable analysis of all patients cohort, there were no significant differences in terms of early stage at presentation (adjusted odds ratio (OR_{adj}) = 0.94, 95% confidence interval (CI) = 0.65–1.37), undergoing lobectomy (OR_{adj} = 0.59, 95% CI = 0.24–1.46), and recurrent-free survival (adjusted hazard ratio (HR_{adj}) =1.20, 95% CI = 0.88–1.65) between groups (UCS/SSS versus CSMBS/PI). However, patients with UCS or SSS had shorter cancer-specific survival (HR_{adj} = 1.61, 95% CI = 1.22–2.15). The results from the propensity score matched patient cohort were not different from those analyses on the full patient cohort.

Conclusion: Thai insurance types have an effect on cancer-specific survival. The Thai government should recognize the importance of these differences, and further multi-center studies with a larger sample size are warranted to confirm this result.

Keywords: Universal Coverage Scheme, Social Security Scheme, Civil Servant Medical Benefit Scheme, cancer death, coverage, pulmonary resection

Introduction

Lung cancer remains an important public health problem and is the leading cause of cancer-related death worldwide. In 2012, 1.6 million patients died of lung cancer[1] and lung cancer was the second most common cause of cancer death in Thailand.[2] In the same year, the National Cancer Institute of Thailand reported that lung cancer

was the most common cancer diagnosed in male Thai patients (16.6%) and the fourth most common cancer diagnosed in female Thai patients (6.6%). If left untreated, the 5-year survival of lung cancer patients is only 6%.[3] However, research has identified a significant difference in recurrence and survival rate between resectable stages (IA-IIIA) of Non-small cell lung cancer (NSCLC) after complete oncologic resection, and in the five-year survival of stage I (70%) and stage III (38%) resectable NSCLC patients.[4]

According to current guidelines, pre-treatment investigation of NSCLC requires advanced procedures such as an endobronchial ultrasound (EBUS), esophageal ultrasound and positron emission tomography-computed tomography (PET-CT), as well as high-cost drugs, targeted drugs and immunotherapy, which can increase the overall cost of treatment. Despite these recommendations, some of these procedures and drugs are not included in certain health-care insurance programs and are not eligible for reimbursement.

Currently, three public health insurance programs are available for the Thai population, including the Civil Servant Medical Benefit Scheme (CSMBS; 9%), the Social Security Scheme (SSS; 16%), and the Universal Coverage Scheme (UCS; 75%).[5] Private health insurance (PI) is another health insurance program that everyone can apply for depending on the plan they choose and the cost they can afford. Overall, the benefits package of CSMBS is slightly higher than those of UCS and SSS (Table 1). For example, CSMBS covers high-cost drugs, targeted drugs and immunotherapy as well as high-cost procedures (EBUS, PET-CT), while UCS and SSS do not. Private health insurance coverage varies by company and depends on patient age and the type of plan they choose (local, international, basic coverage, etc.).

Previous studies have demonstrated that insurance type is significantly associated with surgical outcomes, stage of disease at diagnosis, tumor recurrence and survival,[6–9] while some studies have not reported these differences.[10,11] Although the insurance types available in each country are different, the association between higher coverage and better outcomes has been consistently observed.[12] To our knowledge, this is the first study to report on the impact of insurance type on NSCLC outcomes in the Thai population. The aim of this study was to determine the effect of insurance type on stage at presentation, surgical procedure, tumor recurrence and cancer-specific survival in resectable NSCLC.

Table 1 Characteristics of Thailand's Health Insurance Programs

Insurance Types	Characteristics
(A) CSMBS (9%)	
Target population	Government employees plus dependents including parents, spouses and up to two children aged <20 years
Financing source	General tax, noncontributory scheme
Payment method	Fee for service for outpatient services and conventional DRG for inpatient services
Health delivery	Free choice of public providers, no registration required
Benefits package	Slightly higher than SSS and UCS
B. SSS (16%)	
Target population	Private sector employees, excluding dependents
Financing source	Payroll tax financed, tri-partite contribution 1.5% of salary, equally by employer, employee and government
Payment method	Inclusive capitation for outpatient and inpatient services
Health delivery	Registered public and private competing contractors
Benefits package	Comprehensive: outpatient, inpatient, accident and emergency, high-cost care, with very minimal exclusion list; excludes prevention and health promotion
(A) UCS (75%)	
Target population	The rest of population not covered by SSS and CSMBS
Financing source	General tax
Payment method	Capitation for outpatient services and global budget plus DRG for inpatient services
Health delivery	Registered contractor provider, notably within the district health system
Benefits package	Similar to SSS, including prevention and health promotion for the whole population

Note: Data from Health Insurance System Research Office (HISRO) (2012), Nonthaburi, Thailand.[5]

Abbreviations: CSMBS, Civil Servant Medical Benefit Scheme; SSS, Social Security Scheme; UCS, Universal Coverage Scheme; DRG, diagnosis-related groups.

Patients and Methods

Patient Selection, Treatments and Outcomes

Adult patients (age ≥18 years) with NSCLC who underwent pulmonary resection (either curative or palliative

intent) at Chiang Mai University Hospital from January 2007 through December 2015 were retrospectively reviewed. Patients were divided into two groups based on their benefits package; patients with CSMBS (235 patients, 40.3%) or PI (4 patients, 0.7%) and patients with UCS (311 patients, 53.3%) or SSS (33 patients, 5.7%). The benefits package of CSMBS is slightly higher than SSS and UCS while that of UCS is similar to SSS. The characteristics of Thailand's health insurance programs are shown in Table 1. Private health insurance (PI) is another health insurance program that everyone can apply for depending on the plan they choose and the cost they can afford and its coverage varies by company and depends on patient age and the type of plan they choose (local, international, basic coverage, etc.). Patient characteristics, comorbid diseases, smoking status, pathological stage, tumor characteristics, operative data, post-operative complications, tumor recurrence and cancer-specific survival were extracted from medical records. The primary outcome was cancer-specific survival and the secondary outcomes were differences in stage at presentation, surgical procedure and tumor recurrence between the two groups.

Patients underwent computed tomography (CT) with contrast or whole-body positron emission tomography, bronchoscopy with biopsy, bronchial washing, and brushing or bronchial lavage cytology for preoperative cancer staging. If mediastinal lymph nodes were larger than 1 cm from the CT scan, an EBUS for fine-needle aspiration, or a mediastinoscope biopsy, was performed. Preoperative biochemistry profile, a pulmonary function test, a room-air arterial blood gas, and an electrocardiography were routinely performed.

Patients underwent wedge resection, segmentectomy, lobectomy and pneumonectomy. The indication for sublobar resection (wedge resection or segmentectomy) was made according to the American College of Chest Physicians Evidence-Based Clinical Practice Guidelines.[13] Surgical approaches included open thoracotomy and video-assisted thoracoscopic surgery (VATS). Systematic mediastinal lymph node dissection (SLND) or sampling (SLNS) was performed in all cases. Lymph node ratio was calculated as the proportion of positive dissected lymph node divided by the total amount of dissected lymph nodes. Tumor staging was reviewed according to the 8th edition of the TNM classification for lung cancer issued by the International Association for the Study of Lung Cancer (IASLC).[4] Stage at presentation was categorized into 3 groups; localized (stage I), regional (stage II or III), and distant (stage IV), as previously described by Walker et al.[8]

After discharge, follow-up was performed at 2 weeks and at 1–2 months with a chest x-ray and physical examination, and then every 3 months for the first 2 years, and then every 6 months with a CT scan. When tumor recurrence was suspected, diagnostic procedures were performed to confirm the diagnosis either with cytology or diagnostic radiology. Patients received chemotherapy and/or radiotherapy according to their performance status and tumor status. The regimens of chemotherapy included cisplatin, carboplatin, vinorelbine, vinorelbine, gemcitabine, docetaxel, pemetrexed and targeted therapy (erlotinib, gefitinib, crizotinib) depending on molecular testing and insurance coverage. Overall survival and recurrence-free survival were calculated from the date of surgery to the most recent follow-up contact or to the date of death, and from the date of first tumor diagnosis to either local recurrence or distant metastasis, respectively.

This study was reviewed and approved by the Institutional Review Board of Faculty of Medicine, Chiang Mai University, Chiang Mai, Thailand with Study Code: SUR-2561-05572/Research ID: 5572, and approval ID 238/2018. Patient consent to review their medical records was not required by the Institutional Review Board of the Faculty of Medicine, Chiang Mai University. This study was considered exempt as de-identified data for all analyses. Individual-level data was not used, and all data was kept confidential and in compliance with the Declaration of Helsinki.

Statistical Analysis

Categorical variables were presented as frequencies and proportions; continuous variables were presented as mean ± standard deviation (SD) or median ± interquartile range (IQR). Fisher exact tests were used for comparing categorical data, and unpaired Student's *t*-test or Wilcoxon rank-sum tests were performed for continuous variables. Multiple imputations (MI) with a multivariate normal equation were performed for any variables with at least 10% missing values.[14] Results of the MI analysis were then compared to the results from a complete-case analysis. Cox proportional hazards models were used to examine the impact of insurance type on recurrence and cancer-specific survival. Logistic regressions were performed to assess associations of insurance type with tumor stage at presentation, surgical procedure (lobectomy versus sublobar resection), and surgical approaches (VATS versus open thoracotomy). Any prognostic factors with a p value <0.1 in

the univariable analyses, in addition to other potential clinical confounders associated with stage at presentation, surgical procedures or approaches, tumor recurrence, and cancer-specific survival, were adjusted for in the multivariable Cox proportional hazards model. Multicollinearity of independent factors was tested before performing multivariable analysis. One-to-one propensity score matching was also performed. Logistic regression was used to calculate a propensity score, which evaluates confounding by indication and/or baseline covariates between two insurance groups. The variables included in the propensity score matching model were age, gender, body mass index (BMI), smoking status, comorbid disease, stage of disease, intratumoral lymphatic invasion, intratumoral vessel invasion, visceral pleural invasion, and tumor necrosis. A standardized mean difference (SMD) between groups for all covariates is shown in Table 2. The primary and secondary outcomes for propensity score matched patient cohort were analyzed by multivariable Cox's regression analysis and logistic regression analysis as appropriate. The statistical analysis was completed in STATA (Release 15.1, 2018; StataCorp, CS, TX, USA), with $p < 0.05$ indicating a statistically significant difference.

Results

Patient Characteristics

There were 583 patients diagnosed with resectable NSCLC included in this study; 334 with UCS or SSS and 239 with CSMBS or PI. Patients with UCS or SSS were younger, more likely to be active smokers, had lower BMI, lower percent predicted forced expiratory volume in 1 minute (FEV1), more advanced stage of disease, poorer cell differentiation, were less likely to have hypertension and dyslipidemia, and were more likely to have tumor necrosis (Table 2). There were no statistically significant differences in gender, number of pack-years of smoking, having chronic obstructive pulmonary disease (COPD), diabetes mellitus (DM), history of malignancy, preoperative ECG, ejection fraction, cell types, intratumoral lymphatic and vascular invasion, and having visceral pleural invasion between the two groups. After matching, 224 patients were included in both groups, and almost all covariates were balanced between two groups (Table 2). A standardized mean difference (SMD) of almost all covariates between the two groups after matching was less than 0.2.

Stage at Diagnosis

More patients with CSMB or PI presented with localized disease than did those with UCS or SSS (Figure 1). After adjusting for age, gender, smoking status, and clinical presentation, the adjusted odds ratio of localized disease (early stage) at presentation for UCS or SSS group compared to CSMBS or PI group were 0.94 (95% CI = 0.65–1.37, $p = 0.762$) for the full patient cohort and 0.95 (95% CI=0.63–1.42, $p=0.796$) for the propensity score matched patient cohort.

Surgical Procedures

The percentage of patients undergoing lobectomy between those with UCS or SSS and CSMBS or PI were 82.1% and 73.5%, respectively ($p = 0.041$) (Table 3). However, after adjusting by age, gender, percent predicted FEV1, comorbid diseases, tumor diameter, and stage of disease, this difference was not statistically significant. The adjusted odds ratio of lobectomy for UCS or SSS group compared to CSMBS or PI group was 0.59 (95% CI = 0.24–1.46, $p=0.251$) for the full patient cohort and 0.50 (95% CI=0.19–1.32, $p=0.160$) for the propensity score matched patient cohort (Table 4). There was no significant difference in terms of the type of mediastinal lymph node evaluation between the two groups.

Surgical Approaches

The percentage of patients undergoing VATS approach between those with UCS or SSS and CSMBS or PI were 22.3% and 14.6%, respectively ($p = 0.020$) (Table 3). However, after adjusting by age, gender, percent predicted FEV1, comorbid diseases, tumor diameter, and stage of disease, this difference was not statistically significant. The adjusted odds ratio of VATS approach for UCS or SSS group compared to CSMBS or PI group was 0.99 (95% CI = 0.36–2.72; $p=0.989$) for the full patient cohort and 0.82 (95% CI=0.26–2.55, $p=0.729$) for the propensity score matched patient cohort (Table 4).

Perioperative Outcomes

There were no significant differences in post-operative complications such as pneumonia, re-intubation, arrhythmias, atelectasis, acute renal failure with hemodialysis and air leakage between the two insurance groups. Length of hospital stay was comparable between the two groups, and the median time was 7 days (IQR=5–10 days). Operative time was longer in patients with UCS or SSS (149.8±54.3 minutes versus 138.8±50.1 minutes, respectively; $p = 0.015$). Median

Table 2 Patient Characteristics Before and After Propensity Score Matching According to Insurance Coverage

Variable	Before Propensity Score Matching (Full Patient Cohort)				After Propensity Score Matching (Propensity Score Matched Patient Cohort)			
	UCS or SSS N=344	CSMBS or PI N=239	p-value	SMD	UCS or SSS N=244	CSMBS or PI N=244	p-value	SMD
Age (years), Mean ± SD	61.10±10.70	64.28±9.80	<0.001	0.310	63.9±10.0	62.9±10.6	0.316	0.098
Gender, n (%)			0.864	0.015			0.441	0.082
Female	140 (40.7)	99 (41.4)			95 (42.4)	86 (38.4)		
Male	204 (59.3)	140 (58.6)			129 (57.6)	138 (61.6)		
BMI (kg/m^2), Mean ± SD	20.7±3.6	22.3±3.9	<0.001	0.420	22.0±3.8	21.4±3.5	0.099	0.167
Smoking status, n (%)			<0.001	0.339			0.624	0.056
Non-smokers	60 (17.4)	74 (31.0)			49 (21.9)	68 (30.4)		
Active smoker or ex-smokers	248 (72.1)	145 (60.7)			145 (64.7)	139 (62.1)		
Passive smoking	11 (3.2)	3 (1.3)			10 (4.5)	3 (1.3)		
Unknown	25 (7.3)	17 (7.1)			20 (8.9)	14 (6.2)		
Pack-year, Median (IQR)	25 (12–41.3)	24 (10.5–40)	0.559	−0.189	24 (10.8–40)	30 (15–50)	0.103	−0.317
Comorbid Disease, n (%)								
COPD	48 (14.0)	39 (16.3)	0.479	0.066	38 (17)	32 (14.3)	0.516	0.074
Diabetic mellitus	41 (11.9)	27 (11.3)	0.896	0.019	26 (11.6)	33 (14.7)	0.402	0.093
Hypertension	115 (33.4)	111 (46.4)	0.002	0.268	98 (43.8)	92 (41.1)	0.633	0.054
Dyslipidemia	50 (14.5)	63 (26.4)	0.001	0.296	53 (23.7)	41 (18.3)	0.202	0.132
History of other malignancy	16 (4.7)	20 (8.4)	0.080	0.151	16 (7.1)	14 (6.3)	0.850	0.036
Pulmonary Function Test								
Percent predicted FEV1, Mean ± SD	77.0±21.9	84.2±22.9	0.036	0.322	84.6±23.0	79.8±22.2	0.212	0.212
Preoperative PaO_2, Mean ± SD	127.9±52.9	120.3±49.2	0.609	−0.149	120.1±49.7	123.6±52.1	0.832	−0.069
Preoperative $PaCO_2$, Mean ± SD	49.4±29.9	39.9±12.8	0.198	−0.409	41.6±12.2	47.5±16.2	0.217	−0.412
Preoperative ECG, n (%)			0.106	0.234			0.146	0.247
Normal	233 (67.7)	176 (73.6)			166 (74.10)	151 (67.4)		
ST-T segment abnormality	28 (8.1)	17 (7.1)			16 (7.1)	19 (8.5)		
Bundle branch block	11 (3.2)	13 (5.4)			13 (5.8)	8 (3.6)		
Arrhythmias	8 (2.3)	6 (2.5)			6 (2.7)	6 (2.7)		
Non-specific abnormality	64 (18.6)	27 (11.3)			23 (10.3)	40 (17.9)		
Ejection fraction (%), Mean ± SD	64.4±10.0	67.6±7.4	0.159	0.367	67.6±7.5	64.4±10.2	0.199	0.364
Cell types, n (%)			0.272	0.251			0.952	0.053
Adenocarcinoma	215 (62.5)	167 (69.9)			156 (69.6)	151 (67.4)		
Squamous cell carcinoma	87 (25.3)	45 (18.8)			43 (19.2)	45 (20.1)		
Large cell carcinoma	10 (2.9)	6 (2.5)			5 (2.2)	6 (2.7)		
Other[a]	32 (9.3)	21 (8.8)			20 (8.9)	22 (9.8)		
Tumor staging (8th IASLC edition)			0.016	0.381			0.642	0.252
IA1	6 (1.7)	8 (3.4)			8 (3.6)	5 (2.2)		
IA2	18 (5.2)	29 (12.1)			23 (10.3)	13 (5.8)		
IA3	41 (11.9)	26 (10.9)			24 (10.7)	25 (11.2)		
IB	46 (13.4)	28 (11.7)			28 (12.5)	33 (14.7)		
IIA	25 (7.3)	11 (4.6)			11 (4.9)	16 (7.1)		
IIB	67 (19.5)	43 (18.0)			41 (18.3)	48 (21.4)		
IIIA	92 (26.7)	61 (25.5)			59 (26.3)	55 (24.6)		
IIIB	32 (9.3)	11 (4.6)			11 (4.9)	15 (6.7)		
IIIC	1 (0.3)	2 (0.8)			2 (0.9)	1 (0.5)		
IVA	16 (4.7)	20 (8.4)			17 (7.6)	13 (5.8)		

(*Continued*)

Table 2 (Continued).

Variable	Before Propensity Score Matching (Full Patient Cohort)				After Propensity Score Matching (Propensity Score Matched Patient Cohort)			
	UCS or SSS N=344	CSMBS or PI N=239	p-value	SMD	UCS or SSS N=244	CSMBS or PI N=244	p-value	SMD
Cell differentiation, n (%)			0.009	0.316			0.797	0.108
Well differentiation	88 (29.8)	85 (44.3)			73 (41.2)	68 (37.0)		
Moderately differentiation	128 (43.4)	70 (36.5)			69 (39.0)	79 (42.9)		
Poorly differentiation	70 (23.7)	31 (16.2)			30 (17.0)	30 (16.3)		
Undifferentiation	9 (3.1)	6 (3.1)			5 (2.8)	7 (3.8)		
Intratumoral lymphatic invasion, n (%)	249 (72.4)	173 (72.4)	1.000	<0.001	164 (73.2)	162 (72.3)	0.916	0.020
Intratumoral vascular invasion, n (%)	132 (38.4)	92 (38.5)	1.000	0.003	89 (39.7)	86 (38.4)	0.846	0.027
Visceral pleural invasion, n (%)	64 (18.6)	42 (17.6)	0.827	0.033	40 (17.9)	40 (17.9)	1.000	0.026
Tumor necrosis, n (%)	119 (34.6)	48 (20.1)	<0.001	0.330	47 (21.0)	53 (23.7)	0.571	0.064
Propensity score, Mean±SD	0.65±0.16	0.53±0.16	<0.001	−0.723	0.57±0.12	0.56±0.14	0.615	−0.057

Notes: [a]Other cell types included mucoepidermoid carcinoma, adenoid cystic carcinoma, carcinoid tumor, adenosquamous carcinoma, and neuroendocrine tumor;
Abbreviations: SD, standard deviation; BMI, body mass index; IQR, interquartile range; FEV1,forced expiratory volume in 1 second; PaO_2,partial pressure of oxygen (mmHg); $PaCO_2$,partial pressure of carbon dioxide (mmHg); ECG,electrocardiogram; ST-T, the interval between ventricular depolarization and repolarization from electrocardiogram; CSMBS, Civil Servant Medical Benefit Scheme; SSS, Social Security Scheme; UCS, Universal Coverage Scheme; PI, private health insurance; COPD, chronic obstructive pulmonary disease; SMD, standard mean difference.

amount of blood loss was higher (p <0.001) with UCS or SSS (200 mL, IQR=100–300 mL) than in CSMBS or PI (100 mL, IQR=100–200 mL).

Tumor Recurrence and Cancer-Specific Survival

In the univariable analysis for tumor recurrence, 36 patients (6.2%) diagnosed with stage IVA who were treated with palliative resection due to tumor complications such as obstructive pneumonitis or hemoptysis were excluded for analysis (Table 2). Although tumor recurrence rate was similar between both groups, time to recurrence was significantly shorter in the UCS or SSS group (16.4 months [IQR=6.3–45.7 months] versus 21.7 months [IQR=8.6–50.2 months], respectively; p = 0.013) for the full patient cohort, but not different for the propensity score matched patient cohort (Table 3). Cancer-specific mortality rate was higher in the UCS or SSS group for both patient cohorts (63.9% - 219 patients versus 50.6% - 121 patients; p = 0.002 for the full patient cohort and 62.1%-139 patients versus 50.9%-114 patients; p=0.018 for the propensity score matched patient cohort) (Table 3). In multivariable analyses using multivariable Cox's regression analysis adjusted by age, gender, comorbid disease, smoking status, cell differentiation, cell type, visceral pleural invasion, intratumoral blood vessel invasion, intratumoral lymphatic invasion, perineural invasion, tumor necrosis, tumor stage, surgical approaches, surgical procedures, type of lymph node dissection, tumor recurrence, and chemotherapy (included targeted therapy or immunotherapy), insurance type was not associated with tumor recurrence; the adjusted hazard ratio for tumor recurrence of UCS or SSS group compared to CSMBS or PI group was 1.20 (95% CI=0.88–1.65, p=0.241) for the full patient cohort and 1.11 (95% CI=0.78–1.59, p=0.554) for the propensity score matched patient cohort. However, insurance type was associated with cancer-specific survival; the adjusted hazard ratio for cancer-specific mortality of UCS

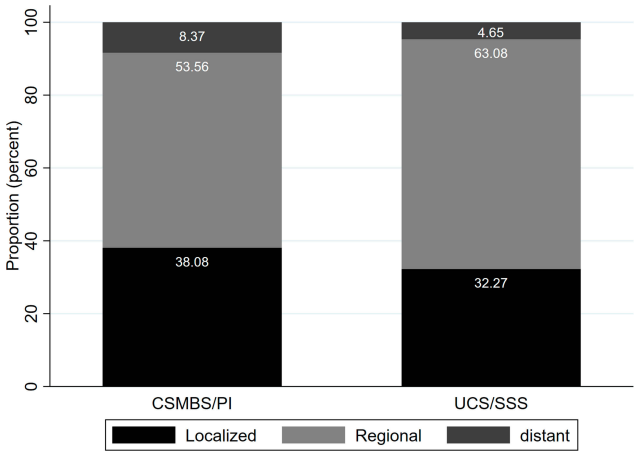

Figure 1 Proportion of patients presenting with localized, regional, or distant diseases according to insurance status (p = 0.034). Stage I disease was considered localized, stage II to III disease was considered regional, and stage IV disease was considered distant.
Abbreviations: CSMBS, Civil Servant Medical Benefit Scheme; SSS,Social Security Scheme; UCS,Universal Coverage Scheme; PI, private insurance.

Table 3 Treatment and Post-Operative Outcomes Between Two Patient Cohort According to Insurance Coverage.

Variable	Full Patient Cohort			Propensity Score Matched Patient Cohort		
	UCS or SSS N=344	CSMBS or PI N=239	p-value	UCS or SSS N=224	CSMBS or PI N=224	p-value
Surgical Procedure, n (%)			0.041			0.479
Wedge resection	44 (12.9)	52 (21.9)		46 (20.6)	34 (15.2)	
Segmentectomy	10 (2.9)	6 (2.5)		6 (2.7)	5 (2.2)	
Lobectomy	280 (82.1)	175 (73.5)		168 (74.9)	181 (80.8)	
Pneumonectomy	7 (2.1)	5 (2.1)		4 (1.8)	4 (1.8)	
Surgical Approach, n (%)			0.020			0.267
Open thoracotomy	292 (85.4)	185 (77.7)		179 (79.8)	189 (84.3)	
Video-assisted thoracoscopic surgery (VATS)	50 (14.6)	53 (22.3)		45 (20.2)	35 (15.7)	
Mediastinal lymph node evaluation, n (%)			0.901			0.977
Lymph node sampling	48 (16.1)	31 (15.5)		33 (14.7)	34 (15.2)	
Systematic lymph node dissection	251 (83.9)	169 (84.5)		29 (13.0)	30 (13.4)	
Lymph node ratio, Median (IQR)	0.2 (0.1–0.4)	0.2 (0.1–0.4)	0.644	162 (72.3)	160 (71.4)	0.675
Chemotherapy[a], n (%)			0.234	0 (0–0.1)	0 (0–0.2)	0.476
No chemotherapy	165 (48.0)	121 (50.6)				
Adjuvant therapy	147 (42.7)	105 (43.9)		113 (50.5)	109 (48.7)	
Neoadjuvant therapy or induction therapy	32 (9.3)	13 (5.4)		98 (43.7)	95 (42.4)	
Operative time (minutes), Mean ± SD	149.8±54.3	138.8±50.1	0.015	13 (5.8)	20 (8.9)	0.288
Estimated blood loss (mL), Median (IQR)	200 (100–300)	100 (100–200)	<0.001	144.9±53.9	139.7±50.0	0.001
ICU stay (hours), Median (IQR)	36.2 (17.8–69.3)	37.2 (18.4–68.2)	0.750	200 (100–300)	100 (100–200)	0.015
Immediate extubation after surgery, n (%)	283 (82.3)	215 (90.0)	0.012	0 (0–17.2)	0 (0–0)	0.093
In-hospital mortality, n (%)	8 (2.3)	3 (1.3)	0.538	188 (83.9)	201 (89.7)	0.221
Postoperative complications, n (%)						
Pneumonia	13 (3.8)	6 (2.5)	0.482	10 (4.5)	5 (2.2)	0.293
Re-intubation	11 (3.2)	4 (1.7)	0.298	8 (3.6)	3 (1.3)	0.221
Atelectasis with bronchoscopy needed	7 (2.0)	7 (2.9)	0.585	4 (1.8)	7 (3.1)	0.544
Arrhythmias	10 (2.9)	5 (2.1)	0.605	7 (3.1)	5 (2.2)	0.771
Air leakage	32 (9.3)	14 (5.9)	0.160	17 (7.6)	14 (6.2)	0.710
Acute renal failure with hemodialysis needed	2 (0.6)	2 (0.8)	1.000	2 (0.9)	2 (0.9)	1.000
Acute pulmonary embolism	1 (0.3)	0	1.000	1 (0.5)	0	1.000
Chylothorax	3 (0.9)	3 (1.3)	0.693	1 (0.5)	3 (1.3)	0.623
Other minor complications	31 (9.0)	15 (6.3)	0.275	20 (8.9)	13 (5.8)	0.278
Composite major complications	43 (12.5)	25 (10.5)	0.513	25 (11.2)	23 (10.3)	0.879
Length of hospital stay (days), Median (IQR)	7 (5–10)	7 (5–10)	0.494	7 (5–9)	7 (5–10)	0.911
Tumor recurrence[b], n (%)	145 (44.2)	100 (45.7)	0.792	93 (44.1)	93 (44.9)	0.922
Recurrence time (months)[b], Median (IQR)	16.4 (6.3–45.7)	21.7 (8.6–50.2)	0.013	11.5 (5.3–21.2)	14.2 (6.4–22.9)	0.183
Cancer-specific mortality, n (%)	219 (63.9)	121 (50.6)	0.002	139 (62.1)	114 (50.9)	0.018
Follow-up time (months), median (IQR)	26.5 (10.0–55.9)	34.6 (17.2–61.3)	0.010	30.0 (11.1–56.3)	34.5 (16.5–61.0)	0.083

Notes: [a]Targeted therapy and immunotherapy were not used as induction therapy or adjuvant setting, [b]Excluded stage IV disease.

Abbreviations: ICU, intensive care unit; IQR, interquartile range; CSMBS, Civil Servant Medical Benefit Scheme; SSS, Social Security Scheme; UCS, Universal Coverage Scheme; PI, private health insurance

or SSS group compared to CSMBS or PI group was 1.61 (95% CI = 1.22–2.15, p=0.001) for the full patient cohort and 1.48 (95% CI=1.08–2.03, p=0.027 for the propensity score matched patient cohort) (Table 4). Kaplan–Meier curves illustrating the recurrent-free survival and cancer-specific survival between insurance types for the full patient cohort are shown in Figure 2 and Kaplan–Meier curves illustrating the cancer-specific survival between insurance types for propensity score matched patient cohort is shown in Supplement Figure A.

Table 4 Differences in Outcomes and Surgical Procedure/Approach for UCS or SSI Vs CSMBS or PI Between Two Patient Cohort

Outcome Variable (UCS or SSI versus CSMBS or PI)	Full Patient Cohort			Propensity Score Matched Patient Cohort		
	Estimate	95% CI	p-value	Estimate	95% CI	p-value
Tumor recurrence	1.20[a]	0.88–1.65	0.241	1.11[a]	0.78–1.59	0.554
Cancer-specific mortality	1.6[a]	1.22–2.15	0.001	1.48[a]	1.08–2.03	0.027
Early stage at presentation	0.94[b]	0.65–1.37	0.762	0.95[b]	0.63–1.42	0.796
Lobectomy procedure	0.59[c]	0.24–1.46	0.251	0.50[c]	0.19–1.32	0.160
VATS approach	0.99[c]	0.36–2.72	0.989	0.82[c]	0.26–2.55	0.729

Notes: [a]Adjusted hazard ratio analyzed by Cox's proportion hazard model adjusted by age, gender, comorbid disease, smoking status, cell differentiation, cell type, visceral pleural invasion, intratumoral blood vessel invasion, intratumoral lymphatic invasion, perineural invasion, tumor necrosis, tumor stage, surgical approaches, surgical procedures, type of lymph node dissection, tumor recurrence, and chemotherapy (included targeted therapy or immunotherapy). Patients with stage IV were excluded in multivariable analysis model for tumor recurrence.
[b]Adjusted odds ratio analyzed by logistic regression analysis adjusting for age, gender, smoking status and clinical presentations (hemoptysis, chronic cough, significant weight loss, poor appetite, chest pain, and dyspnea on exertion). [c]Adjusted odds ratio analyzed by logistic regression analysis adjusting for age, gender, % predicted FEV1, comorbid diseases, smoking status, tumor diameter, and stage of disease.
Abbreviations: CSMBS, Civil Servant Medical Benefit Scheme; SSS, Social Security Scheme; UCS, Universal Coverage Scheme; PI, private health insurance; CI, confidence interval; VATS, video-assisted thoracoscopic surgery.

In summary, the results from the propensity score matched patient cohort analysis were not different from the full patient cohort analysis.

Discussion

This study evaluated the association between health insurance, stage at presentation, surgical treatment and outcomes among a group of NSCLC patients in northern Thailand. Currently, UCS or SSS coverage is provided for 75% of the Thai population while CSMBS is provided for government officials and provides coverage after retirement. Additionally, PI is provided for all patients who are willing to pay for non-government health insurance.

This analysis revealed differences between the two groups on the full patient cohort analysis; UCS or SSS patients were younger and had lower mean BMI than those with CSMBS or PI. However, BMI values in both groups were within the "normal" range. CSMBS or PI patients had more comorbid diseases such as COPD, hypertension and dyslipidemia. This may relate to the older age of CSMBS or PI patients (64.28±9.80 years vs 61.10±10.70 years, $p<0.001$). There were a greater number of active- and former smoking patients in the UCS or SSS group than in the CSMBS or PI group, and this may explain why percent predicted FEV1 in the UCS or SSS group was lower compared to the CSMBS or PI group.

Consistent with previous research, the most common cancer type observed here was adenocarcinoma (65.52%), followed by squamous cell carcinoma (22.64%).[9,15,16] Variability in stage at presentation, tumor aggressiveness, mean recurrence time and overall survival among insurance types has been documented among lung cancer

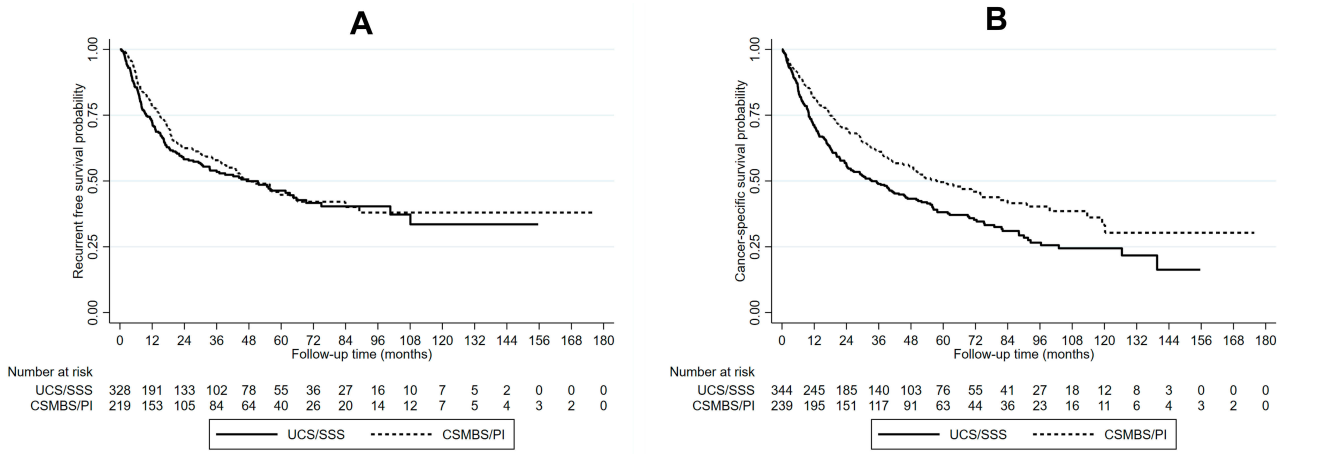

Figure 2 Kaplan–Meier curves illustrating (**A**) recurrent-free survival (p = 0.538) (excluded stage IV disease) and (**B**) cancer-specific survival (p=0.001) between insurance types (CSMBS, Civil Servant Medical Benefit Scheme; SSS, Social Security Scheme; UCS, Universal Coverage Scheme; PI, private insurance).

patients.[9,17,18] Here, we observed that the proportion of patients who presented with localized disease was higher in the CSMBS or PI group in univariable analyses, but this difference was not significant after adjusting for other confounding factors. Previous studies have demonstrated that both patients with insurance that provides less medical coverage and patients with no insurance were associated with more advanced disease at presentation and poorer long-term outcomes.[8,9,19,20] These studies also reported that insurance status was associated with a shorter cancer-specific survival and an average time to recurrence. A systematic review of 23 articles stated that American patients with Medicaid or no insurance had a higher stage-specific and overall mortality rate.[21] There were several reasons that survival might be impacted by insurance status. First, lung cancer survival depends on disease stage and treatment type; for example, chemotherapy regimen and targeted therapy are associated with a higher cancer-specific survival.[22,23] Second, in terms of access to medical service, most UCS or SSS patients reside in rural areas in northern Thailand. In general, lower education, lower socioeconomic status, and transit burden of this population result in reduced access to medical care, delays in proper management of their cancer, and loss to follow-up care. Previous studies from other countries have found that insurance type effects accessing medical care.[9,24,25] Third, insurance type can be a limitation to diagnostic workup and treatment; high-cost invasive and non-invasive procedures such as EBUS, PET-CT scans, some chemotherapy regimen (high-cost drug), targeted therapy and immunotherapy are not covered by UCS or SSS. Therefore, patients with UCS or SSS have to pay out of pocket for these services and cannot receive reimbursement. In reality, most of these patients cannot make these payments. Instead, patients with UCS or SSS are treated with low-cost chemotherapy regimens instead of targeted therapy or high-cost drug regimens. Even though targeted and immunotherapy data were not available in this dataset and not included in the multivariable analysis model, these therapies were only used in patients with CSMBS/PI depended on molecular testing. This study found that Thai insurance effected on cancer-specific survival. Patients with UCS or SSS were more likely to have shorter survival than those with CSMBS or PI, both on the full patient cohort analysis and on the propensity score matched patient cohort analysis.

This study found that insurance type was not associated with surgical procedures or surgical approaches in multivariable models. The proportion of patients who underwent a VATS approach was lower in the UCS or SSS group. Before 2009, the stapler devices used were not covered by UCS or SSS but covered by CSMBS or PI with a co-payment. After 2009, these devices were covered by all insurance types. We also found that the operative time and intra-operative blood loss were greater in UCS or SSS group, which may be a consequence in the operative approach. The proportion of open thoracotomy was higher in UCS or SSS group. VATS approach can minimize operative time and intra-operative blood loss as shown in many previous studies.[26–29]

This study has limitations including its retrospective nature and the possibility of selection bias. All patients were fit for surgery, so patients treated with chemotherapy or radiotherapy alone were not included. Although the UCS, SSS, and CSMBS coverage were developed by the Thai government and available to use in all areas of Thailand, Chang Mai University Hospital is a single-tertiary care center that may not represent the heterogeneity in lung cancer treatment found in other institutes. Similarly, the patient population of northern Thailand patients may be different from other areas. Therefore, results of this study may not be generalizable to all other areas in Thailand. Other causes of death such as trauma were not included in the dataset; therefore, we cannot analyze overall survival. Because the median follow-up time is only 30 months, this study presented only the short-term results of NSCLC patients who received primary surgery as their first treatment. Further studies with longer follow-up time are warranted to confirm the results. Finally, there are some unknown prognostic factors such as socioeconomic, lifestyle, occupational or other patient characteristics, as well as treatments including targeted therapy, immunotherapy and radiotherapy that are associated with tumor recurrence or cancer-specific survival that were not included in the multivariable analysis model, as they could not be incorporated from this data.

Conclusions

Thai NSCLC patients with UCS or SSS coverage were more likely to have shorter cancer-specific survival than those with CSMBS or PI. Differences in coverage provided by each insurance type, especially in terms of pre-operative investigation, chemotherapy regimens, targeted therapy and immunotherapy may be associated with cancer-specific survival of these patients. The Thai government should recognize the importance of these differences,

and further multi-center studies with a larger sample size are warranted to confirm this result.

Disclosure

The authors report no conflicts of interest in this work. An abstract of this paper was presented at the 19th World Conference on Lung Cancer (WCLC) as a poster presentation. The poster's abstract was published in 'Poster Abstracts' in the Journal of Thoracic Oncology (https://www.jto.org/article/S1556-0864(18)32428-6/fulltext).

References

1. Ferlay J, Soerjomataram I, Dikshit R, et al. Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012. *Int J Cancer*. 2015;136(5):E359–E86. doi:10.1002/ijc.29210
2. Thailand IHPPi. *Regional Differences in Burden of Disease in Thailand*. Nontaburi: The graphico system limied; 2012.
3. Raz DJ, Zell JA, Ou SI, et al. Natural history of stage I non-small cell lung cancer: implications for early detection. *Chest*. 2007;132(1):193–199. doi:10.1378/chest.06-3096
4. Goldstraw P, Chansky K, Crowley J, et al. The IASLC lung cancer staging project: proposals for revision of the TNM stage groupings in the Forthcoming (Eighth) Edition of the TNM classification for lung cancer. *J Thorac Oncol*. 2016;11(1):39–51. doi:10.1016/j.jtho.2015.09.009
5. Health Insurance System Research Office (HISRO). *Thailand's Universal Coverage Scheme: Achievements and Challenges. An Independent Assessment of the First 10 Years (2001–2010)*. Nonthaburi, Thailand: HISRO; 2012. Available from: http://www.hisro.or.th/main/modules/research/attachgovernance/177/Full-text.pdf. Accessed May 4, 2020.
6. Groth SS, Al-Refaie WB, Zhong W, et al. Effect of insurance status on the surgical treatment of early-stage non-small cell lung cancer. *Ann Thorac Surg*. 2013;95(4):1221–1226. doi:10.1016/j.athoracsur.2012.10.079
7. Hardy D, Liu -C-C, Xia R, et al. Racial disparities and treatment trends in a large cohort of elderly black and white patients with nonsmall cell lung cancer. *Cancer*. 2009;115(10):2199–2211. doi:10.1002/cncr.24248
8. Walker GV, Grant SR, Guadagnolo BA, et al. Disparities in stage at diagnosis, treatment, and survival in nonelderly adult patients with cancer according to insurance status. *J Clin Oncol*. 2014;32(28):3118–3125. doi:10.1200/JCO.2014.55.6258
9. Tantraworasin A, Taioli E, Liu B, et al. The influence of insurance type on stage at presentation, treatment, and survival between Asian American and non-Hispanic White lung cancer patients. *Cancer Med*. 2018;7(5):1612–1629. doi:10.1002/cam4.1331
10. Elchoufani SE, Efird JT, O'Neal WT, et al. The relation of race and type of health insurance to long-term risk of mortality among lung cancer patients in rural Eastern North Carolina. *NC Med J*. 2013;74(6):464–469.
11. Efird JT, Landrine H, Shiue KY, et al. Race, insurance type, and stage of presentation among lung cancer patients. *SpringerPlus*. 2014;3(1):710. doi:10.1186/2193-1801-3-710
12. Sommers BD, Gawande AA, Baicker K. Health insurance coverage and health - what the recent evidence tells us. *N Engl J Med*. 2017;377(6):586–593. doi:10.1056/NEJMsb1706645
13. Howington JA, Blum MG, Chang AC, et al. Treatment of stage I and II non-small cell lung cancer: diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians evidence-based clinical practice guidelines. *Chest*. 2013;143(5 Suppl):e278S–e313S. doi:10.1378/chest.12-2359
14. Rubin DB, Schenker N. Multiple imputation in health-care databases: an overview and some applications. *Stat Med*. 1991;10(4):585–598. doi:10.1002/sim.4780100410
15. 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(2):294–299. doi:10.1002/ijc.21183
16. Field R, Smith B, Platz C, et al. Lung cancer histologic type in the surveillance, epidemiology, and end results registry versus independent review. *J Natl Cancer Inst*. 2004;96(14):1105–1107. doi:10.1093/jnci/djh189
17. Li X, Zhou Q, Wang X, et al. The effect of low insurance reimbursement on quality of care for non-small cell lung cancer in China: a comprehensive study covering diagnosis, treatment, and outcomes. *BMC Cancer*. 2018;18(1):683. doi:10.1186/s12885-018-4608-y
18. Stokes SM, Wakeam E, Swords DS, et al. Impact of insurance status on receipt of definitive surgical therapy and posttreatment outcomes in early stage lung cancer. *Surgery*. 2018;164(6):1287–1293. doi:10.1016/j.surg.2018.07.020
19. Ou SHI, Zell JA, Ziogas A, et al. Low socioeconomic status is a poor prognostic factor for survival in stage I nonsmall cell lung cancer and is independent of surgical treatment, race, and marital status. *Cancer*. 2008;112(9):2011–2020. doi:10.1002/cncr.23397
20. Yorio JT, Yan J, Xie Y, et al. Socioeconomic disparities in lung cancer treatment and outcomes persist within a single academic medical center. *Clin Lung Cancer*. 2012;13(6):448–457. doi:10.1016/j.cllc.2012.03.002
21. Slatore CG, Au DH, Gould MK. An official American Thoracic Society systematic review: insurance status and disparities in lung cancer practices and outcomes. *Am J Respir Crit Care Med*. 2010;182(9):1195–1205. doi:10.1164/rccm.2009-038ST
22. Kenmotsu H, Ohde Y, Wakuda K, et al. Survival data for postoperative adjuvant chemotherapy comprising cisplatin plus vinorelbine after complete resection of non-small cell lung cancer. *Cancer Chemother Pharmacol*. 2017;80(3):609–614. doi:10.1007/s00280-017-3400-z
23. Mok TS, Cheng Y, Zhou X, et al. Improvement in overall survival in a randomized study that compared dacomitinib with gefitinib in patients with advanced non-small-cell lung cancer and EGFR-activating mutations. *J Clin Oncol*. 2018;36(22):2244–2250. doi:10.1200/JCO.2018.78.7994
24. Esnaola NF, Gebregziabher M, Knott K, et al. Underuse of surgical resection for localized, non–small cell lung cancer among whites and African Americans in South Carolina. *Ann Thorac Surg*. 2008;86(1):220–227. doi:10.1016/j.athoracsur.2008.02.072
25. Cheung MC, Hamilton K, Sherman R, et al. Impact of teaching facility status and high-volume centers on outcomes for lung cancer resection: an examination of 13,469 surgical patients. *Ann Surg Oncol*. 2009;16(1):3–13. doi:10.1245/s10434-008-0025-9
26. Rueth NM, Andrade RS. Is VATS lobectomy better: perioperatively, biologically and oncologically? *Ann Thorac Surg*. 2010;89(6):S2107–11. doi:10.1016/j.athoracsur.2010.03.020
27. Scott WJ, Allen MS, Darling G, et al. Video-assisted thoracic surgery versus open lobectomy for lung cancer: a secondary analysis of data from the American College of Surgeons Oncology Group Z0030 randomized clinical trial. *J Thorac Cardiovasc Surg*. 2010;139(4):976–81; discussion 81–3. doi:10.1016/j.jtcvs.2009.11.059
28. Higuchi M, Yaginuma H, Yonechi A, et al. Long-term outcomes after video-assisted thoracic surgery (VATS) lobectomy versus lobectomy via open thoracotomy for clinical stage IA non-small cell lung cancer. *J Cardiothorac Surg*. 2014;9:88. doi:10.1186/1749-8090-9-88
29. Tomaszek SC, Cassivi SD, Shen KR, et al. Clinical outcomes of video-assisted thoracoscopic lobectomy. Mayo Clinic Proceedings; 2009: Elsevier.