Lung Cancer in Patients who Presented with Lung Nodules or Lung Masses at Chest Clinic, Phrae Hospital 2013-2016

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ABSTRACT

Background: Lung cancer is the most common cancers in the world.[1-2] The symptoms often do not appear until the disease is advanced stage and the prognosis is often poor. Prevalence of lung cancer was high in the northern part of Thailand due to smoking risk and seasonal air pollution.[3] Symptoms of lung cancer include coughing, unexplained weight loss, shortness of breath and chest pain.[4] There are 2 major histological types of primary lung cancer, about 85% are non-small cell lung cancer (NSCLC) which usually grows and spreads slowly, and about 15% small cell lung cancer (SCLC) which is fast growing and can spread quickly.[5] There has been no previous study to evaluate prevalence of lung cancer in patients who presented with lung nodules or masses at Phrae Hospital.

Objective: The primary aim of this study was to find the prevalence of lung cancer in patients who presented with lung nodules or lung masses and underwent bronchoscopy from 2013-2016 at the chest clinic of Phrae Hospital and the other aims were to find the risk factors and risk associated lung cancer, type of lung cancer and treatment.

Methods: Observational cross sectional study was carried out from November 2013 to June 2016 at the chest clinic of Phrae Hospital. Patients of both sexes whose age was more than 18 years who had lung nodules or lung masses from CXR or chest CT scan and underwent bronchoscopy with transbronchial pulmonary biopsy, which had final pathology reports were enrolled. All data were collected from OPD cards and computer based database and were completely recorded in case record form.

Results: In total 100 patients who presented with lung nodules or lung masses from CXR or chest CT scan with were enrolled in this study. Seventeen patents were excluded and 83 patients met inclusion criteria and entered into the study. There were 57 male patients (68.7%) and 26 female patients (31.3%). There were 67 smoking patients (80.7%) and 16 non smoking patients (19.3%).The prevalence of lung cancer in patients who presented with lung nodules or lung masses at the chest clinic of Phrae Hospital was 51.8% (41.8-61.8; 95%CI). Smoking was a significant risk factor for lung cancer in this study p-value = 0.031, RR= 3.698 (1.069-12.795; 95%CI) and 88.37% of those who had NSCLC while 11.63% were SCLC. Most patients in lung cancer group were treated with chemotherapy, 28 patients (65.1%).

Conclusion: Prevalence of lung cancer among patients who presented with lung nodules or lung masses at the chest clinic of Phrae Hospital was 51.8%. Smoking was a significant risk factor for lung cancer. The basic information from this study might be beneficial to physicians for lung cancer management and performing lung cancer study in the future.

Keywords: Non-small cell lung cancer (NSCLC); small cell lung cancer (SCLC) (Siriraj Med J 2017;69: 238-246)

INTRODUCTION

Lung cancer is the most common cancer and the main leading cause of death in the world.[1] The prognosis for five years survival rate is very low. From the previous study for all over the world the average five years survival rate after diagnosis was only 10-20%. In Thailand five

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year survival rate was less than 10%.[1-2] From WHO report of all cancers worldwide in 2012, lung cancer was the most common cancer worldwide contributing 13% of the total number of new cases diagnosed in 2012. There were about 14 million lung cancer patients for all over the world in 2012, and 7.4 million of them were male and 6.7 million were female.[6] In Thailand lung cancer was the second most common cancer in male and the fifth most common cancer in female in 2012. There were 402 new cases of lung cancer in 2012, and 61.9% of them were male and 38.1% were female.[7-8] Prevalence of lung cancer was quite high in the northern part of Thailand due to smoking risk and seasonal pollution.[3] Smoking is one of the strongest risk factors for lung cancer.[9] The symptoms often do not appear until the disease is advanced and the prognosis is often poor. Symptoms of lung cancer include coughing, unexplained weight loss, shortness of breath and chest pain.[4] There are 2 major histological types of primary lung cancer, about 85% are non-small cell lung cancer (NSCLC) which usually grows and spreads slowly and about 15% small cell lung cancer (SCLC) which is fast growing and can spread quickly.[5] Although the incidence of lung cancer is increasing each year, most cases were diagnosed when the disease was in advanced stage. The early detection of lung cancer is very important for good prognostic outcome. Physicians should be aware for lung cancer in patients who have abnormal imaging before their symptoms present. A previous study revealed the age of patients and tumor size were the main significant risk factors for predicting probability of lung cancer. Patients with age more than 50 year-old had probability for lung cancer more than 43%[10] and patients who had tumor size more than 2 centimeters had probability for lung cancer more than 50%.[11-12] Not all patients who have lung nodules or lung masses have primary lung cancer, because there are other causes for lung nodules or lung masses such as benign lung tumor, metastases from other origins, pulmonary tuberculosis, lung abscess, or arteriovenous malformation.[13] Previous study also revealed the diagnostic sensitivity for malignant lesions of patients who underwent bronchoscopy with transbronchial pulmonary biopsy was about 53.9%.[14] There was no previous study to evaluate prevalence of lung cancer in patients who presented with lung nodules or masses at Phrae Hospital, Thailand. The primary objective of this study was to evaluate prevalence of lung cancer in patients who presented with lung nodules or masses at the chest clinic, Medicine unit, Phrae Hospital. The other aims were to evaluate risk factors, type of lung cancer and treatment of lung cancer in this study.

MATERIALS AND METHODS

This study was conducted at Chest Clinic, Medicine Unit, Phrae Hospital. Observational cross sectional study was carried out from November 2013 to June 2016. Patients of both sexes whose ages were more than 18 years who had lung nodules or lung masses from CXR or chest CT scan and underwent bronchoscopy with transbronchial pulmonary biopsy, and who had final pathology reports were enrolled. Patients who were diagnosed pulmonary tuberculosis or sputum AFB or sputum culture for mycobacterium tuberculosis positive within 6 months before study were excluded. Patients who could not be completely performed bronchoscopy for tissue biopsy and did not have final pathology reports were also excluded. All data were collected from OPD cards and computer based database and were completely recorded in case record form which revealed all the following data: general information which included hospital number (HN), age, sex, weight, smoking status (pack-year), family history of lung cancer, and symptoms included cough, hemoptysis, dyspnea, weight loss, fever, hoarseness, pleuritic chest pain, lymphadenopathy, tumor location included right upper lobe (RUL), right middle lobe (RML), right lower lobe (RLL), left upper lobe (LUL), and left lower lobe (LLL), tumor size, lung cancer staging of NSCLC which was classified by using the TNM classification for staging of NSCLC[15-16] into stages IA,IB,IIA,IIB,IIIA,IIIB and IV and SCLC which was classified by using clinical staging of SCLC[17-18] into limited and extensive stage, pathology reports of lung cancer were classified by using WHO histological classification[19] and pathology report for non malignancy causes such as granuloma or inflammation, bronchoalveolar larvage (BAL) reports included gram stain (G/S), culture/ sensitivity (C/S), Acid fast bacilli (AFB), C/S for mycobacterium and cytology. All data were descriptively analyzed by using the Statistical Package for Social Sciences (SPSS). Mean, standard deviation, percentage, student-t test, Chi-square test, multivariate analyses and relative risk (RR) were analyzed, and p- value < 0.05 was considered statistically significant.

RESULTS

Between November 2013 and June 2016, in total 100 patients who presented with lung nodules or lung masses from CXR or chest CT scan were enrolled in this study. Seventeen patents were excluded due to sputum AFB positive in 5 patients, could not be performed bronchoscopy in 8 patients and couldn't be performed lung biopsy in 4 patients. In total 83 patients met inclusion criteria and entered into the study. There were 57 male patients (68.7 %) and 26 female patients (31.3 %). The

mean age of patients was 62.17±9.37 years, 57 patients (68.67%) live in rural region and 2 patients (2.4%) had family history of lung cancer (Table 1). The prevalence of lung cancer in patients who presented with lung nodules or lung masses at chest clinic, Phrae Hospital was 51.8% (41.8-61.8; 95%CI). In lung cancer group there were more male patients with statistical significance (p-value= 0.010). The most frequent clinical presentation in this study was cough (62.70%) and other symptoms were weight loss, hemoptysis, pleuritic chest pain, dyspnea, fever and hoarseness respectively (Table 2). In this study there were 68 patients (81.9%) who had history of smoking and 53 patients (77.9%) were male. Smoking was significant risk factor for lung cancer in this study (Table 3) with p-value = 0.031, RR= 3.698 (1.069-12.795; 95%CI). This study showed smoking status in pack-year associated with risk of lung cancer (Fig 1). Most patients had history of smoking 20-30 pack-year (28.9%), only 1 patients had smoking history > 40 pack year (1.2%). Patients who had smoked 10-15 and 20-30 pack-years had statistically significant risk for lung cancer p-values = 0.009 and 0.029 respectively. Patients who had smoked 10-15, 20-30 and > 40 pack-years had relative risk for lung cancer 11, 4.6 and 1.6 respectively.

TABLE 1. Clinical characteristics of the patients with lung nodules or lung masses.

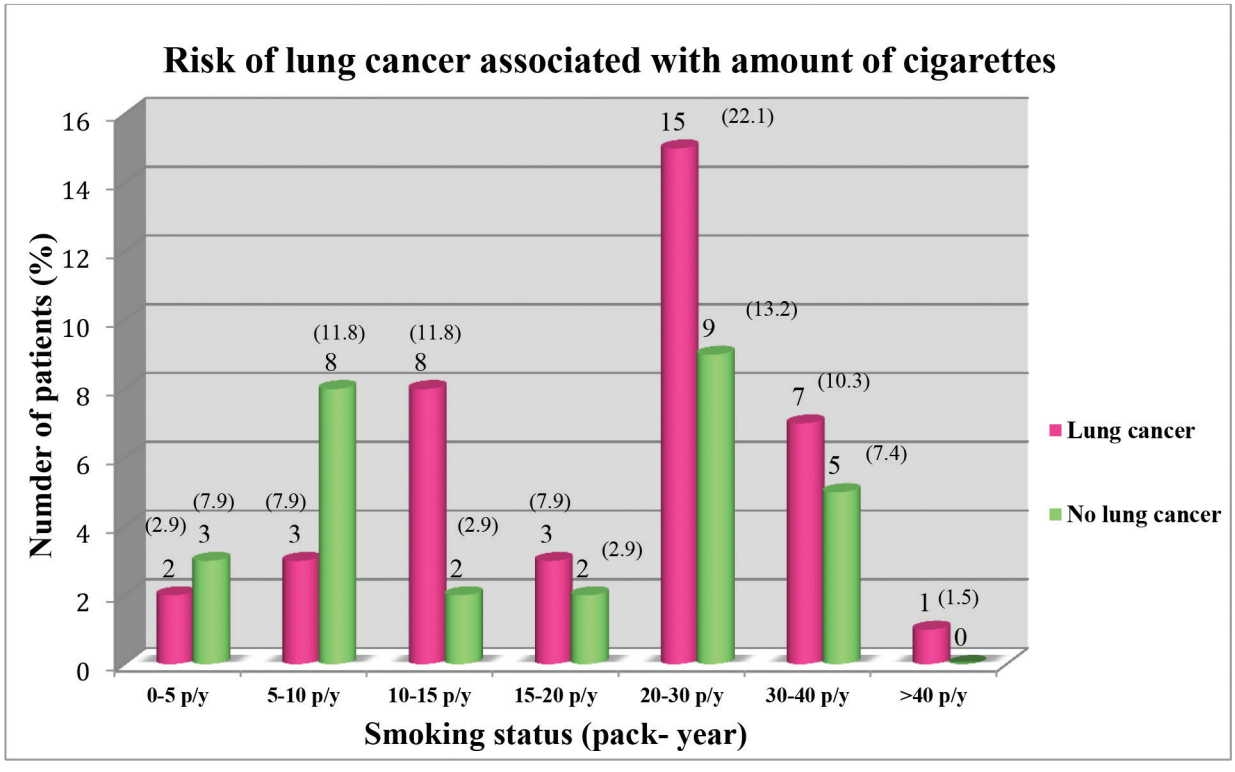
Characteristic	Total (n = 83)	Lung CA group (n= 43)	Non lung CA group (n = 40)	p-value
Age (year, mean±SD) Min 44, Max 85	62.17±9.37	61.72±8.86	62.65±9.98	0.708
Sex, n (%)				
Male	57 (68.70)	35 (81.40)	22 (55.00)	0.010*
Female	26 (31.30)	8 (18.61)	18 (45.00)	0.010*
Domicile (%)				
Urban region	26 (31.33)	14 (32.56)	12 (30.00)	0.802
Rural region	57 (68.67)	29 (67.44)	28 (70.00)	0.802
Family history of Lung cancer, n (%)	2 (2.40)	1 (2.33)	1 (2.50)	1.000

TABLE 2. Clinical presentations of the patients with lung nodules or lung masses.

Presentations	Total (n=83)	Lung CA group (n=43)	Non lung CA group (n=40)	p-value
Cough, n (%)	52 (62.70)	28 (65.11)	24 (60.00)	0.630
Hemoptysis, n (%)	18 (21.71)	9 (20.93)	9 (22.50)	0.862
Dyspnea, n (%)	7 (8.43)	6 (13.95)	1 (2.50)	0.061
Fever, n (%)	3 (3.61)	2 (4.65)	1 (2.50)	0.600
Weight loss, n (%)	42 (50.60)	20 (46.51)	22 (55.00)	0.440
Pleuritic chest pain, n (%)	17 (20.48)	9 (20.93)	8 (20.00)	0.916
Hoarseness, n (%)	3 (3.61)	3 (6.98)	0 (0.00)	0.089
Lymphadenopathy, n (%)	1 (1.20)	0 (0.00)	1 (2.50)	0.297

TABLE 3. Smoking status and lung cancer.

Group	Smoker	Non smoker	Total (n=83)	Statistic values
Lung cancer, n (%)	39 (57.40)	4 (26.70)	43 (51.80)	p-value = 0.031
Non lung cancer, n (%)	29 (42.60)	11 (73.30)	40 (48.20)	RR = 3.698
Total (n=83)	68 (100)	15 (100)	83 (100)	95%CI = 1.099-12.975



Statistic values	Smoking status (pack years) 0-5	5-10	10-15	15-20	20-30	30-40	>40
p-value	0.573	0.973	0.009*	0.176	0.029*	0.096	0.126
RR	1.833	1.031	11.00*	4.125	4.583*	0.761	1.620*
95% CI	0.219-15.333	0.179-5.948	1.603-75.502	0.493-34.499	1.117-18.803	0.761-19.468	1.620-8.679

Fig 1. Smoking status (pack-year) associated with risk of lung cancer.

The most common tumor location that was found in this study was LUL, 27 patients (32.53%) and the least was LLL, 7 patients (8.43%). Tumor location was not statistically significantly related with lung cancer in this study (Table 4). Tumor size 5 - < 7 and > 7 centimeters (cm) were the most common tumor size, 26 patients (31.3%) and tumor size < 2 cm was the least, 1 patient (1.2%). Tumor size > 7 cm was statistically significant risk for lung cancer with p-value = 0.002, but tumor size 3 - < 5 cm was statistically significantly found in patients with no lung cancer in this study p-value = 0.049 (Table 5).

In this study from a total of 83 patients, there were 43 patients (51.8%) who had final pathology report that revealed lung cancer. These 43 patients who had lung cancer were classified into 2 types NSCLC and SCLC. There were 36 patients (87.7%) who had NSCLC and the

TABLE 4. Tumor location of the patients with lung nodules or lung masses.

Tumor location	Total N (%) n= 83	Lung cancer Group N (%) n= 43	Non Lung cancer Group N (%) n= 40	p-value
RUL	22 (26.50)	10 (23.25)	12 (30.00)	0.487
RML	11 (13.25)	4 (9.30)	7 (17.50)	0.273
RLL	16 (19.28)	10 (23.25)	6 (15.00)	0.341
LUL	27 (32.53)	14 (32.55)	13 (32.50)	0.995
LLL	7 (8.43)	5 (11.62)	2 (5.00)	0.278

TABLE 5. Tumor size of the patients with lung nodules or lung masses.

Tumor size (cm.)	Total N (%) n= 83	Lung cancer Group N (%) n= 43	Non Lung cancer Group N (%) n= 40	p-value
≤ 2	1 (1.20)	0 (0.00)	1 (2.50)	0.297
2 - ≤ 3	7 (8.43)	3 (6.98)	4 (10.00)	0.620
3 - ≤ 5	21 (25.30)	7 (16.28)	14 (35.00)	0.049*
5 - ≤ 7	26 (31.32)	11 (25.58)	15 (37.50)	0.242
> 7	26 (31.32)	20 (46.51)	6 (15.00)	0.002*
Multiple nodules	2 (2.41)	2 (4.65)	0 (0.00)	0.167

most common histological type was adenocarcinoma which was found in 22 patients (51.2%), squamous cell carcinoma 7 patients (16.3%), poorly differentiated carcinoma 4 patients (9.4%) and adenosquamous cell carcinoma 3 patients (9.4%). There were 5 patients (11.6%) who had SCLC and 2 patients (4.7%) who had atypical cell suggestive of malignancy (Table 6). For the other 40 patients who had no lung cancer, the pathology report

TABLE 6. Histological types of patients with lung cancer.

Histological type	Number (Total n=43)	%
Adenocarcinoma	22	51.16
Squamous cell carcinoma	7	16.28
Poorly differentiated carcinoma	4	9.30
Adenosquamous cell carcinoma	3	6.98
Small cell carcinoma	5	11.63
Atypical cell suggestive malignancy	2	4.65

showed granuloma in 8 patients (20%), inflammation in 4 patients (10%), fibrosis in 3 patients (7.5%), eosinophillic pneumonia in 1 patient (2.5%) and sarcoma in 1 patient (2.5%). There were 23 patients (57.5%) who had pathology reports that showed negative for granoloma or malignancy.

For BAL reports showed G/S positive in 3 patients (3.6%), which were gram positive cocci 2 patients and gram positive diplococci 1 patient. AFB was positive in 1 patient (1.2%), and C/S was positive in 2 patients (2.4%), which were Staphylococcus aureus 1 patient and Streptococcus pneumoniae 1 patient and C/S for Mycobacterium tuberculosis positive 4 patients (4.8%). Cytology report was found positive in 3 patients, which were NSCLC 2 patients (2.4%) and squamous cell lung cancer 1 patient (1.2%).

The 43 patients (51.8%) with lung cancer who had NSCLC were classified into 4 stages (Table 7). The most stage found in this study was stage IV, 15 patients (39.5%) and no patient in stage IIa in this study. Patients who had SCLC were classified into 2 stages. 4 patients (80%) had limited stage and 1 patient had extensive stage (20%).

TABLE 7. Lung cancer staging of patients with non-small cell lung cancer (NSCLC).

Stage	Number (Total n=38)	%
Ia	1	2.63
Ib	4	10.53
IIa	0	0.00
IIb	1	2.63
IIIa	7	18.42
IIIb	10	26.32
IV	15	39.47

Treament and management in all patients in this study are shown in Table 8. Most cases of patients in lung cancer group were treated with chemotherapy, 28 patients (65.1%). Four 4 patients (9.3%) died during this study. In non lung cancer group 8 patients (20%) denied further investigation and were treated with palliative care treatment. Six patients (15%) were referred for further investigation and all of them underwent surgery and pathology report showed no malignancy such as fibrosis or lung atelectasis. Five patients (12.5%) developed brain metastasis, but no tissue histology to confirm that were primary lung cancer or metastases and all of them were treated with WBRT and palliative care. Two patients (5%) had stable imaging or resolved after 1 year follow up. Four patients (10%) were lost to follow up. Thirteen patients (32.5%) were treated as pulmonary tuberculosis with anti-TB drugs, because one of them had BAL C/S for TB positive (pathology report showed inflammation) and eight of them had pathology report that showed granuloma (one of them had BAL AFB positive, three of them had BAL C/S for TB positive) and four of them which pathology reports were negative, but clinically suggestive pulmonary TB and contact risk for pulmonary TB. All 13 patients who were treated with anti- TB drugs were clinical response and CXR resolved. One patient (2.5%) whose pathology report showed eosinophilic pneumonia was treated with corticosteroid with clinical response and CXR resolved. One patient (2.5%) whose pathology report showed sarcoma was treated with surgery and chemotherapy. Three patients (7.5%) died during this study.

DISCUSSION

This study aimed to find lung cancer in patients who presented with lung nodules or lungs masses, because not all lung nodules or lungs masses are lung cancer, but there are other causes such as lymphoma, sarcoma, metastases from other origins or benign lung tumor like harmatoma and other benign causes such as lung abscess, tuberculosis, arteriovenous malformation and lipoid pneumonia.[13] In this study there were 87 patients who met inclusion criteria, and 43 patients (51.8%) were

TABLE 8. Treatment and Management of all the patients with lung nodules or lung masses.

Lung cancer group		
Treatment and Management	**Number (Total n=43)**	**%**
Chemotherapy	28	65.12
Surgical + Chemotherapy	5	11.63
Chemotherapy + Radiation	3	6.98
Radiation	1	2.33
Palliative care	6	13.95
Dead	4	9.30

Non lung cancer group		
Treatment and Management	**Number (Total n=40)**	**%**
Denied for further investigation, palliative care treatment	8	20.00
Refer for further investigation and management (all patients underwent surgery, pathology reports showed no malignancy)	6	15.00
Developed brain metastasis but no tissue histology confirmation, were treated with WBRT and palliative care	5	12.50
Follow up imaging stable or resolved > 1 year	2	5.00
Loss to follow up	4	10.00
Pulmonary TB treatment, all clinical improved and CXR resolved	13	32.50
Eosinophilic pneumonia was treat with steroid, clinical improved and CXR resolved	1	2.50
Sarcoma was treated with Surgical + Chemotherapy	1	2.50
Dead	3	7.50

diagnosed with lung cancer, which was confirmed by pathology reports and cytology reports. From previous study the diagnostic sensitivity for malignant lung lesion was 53.9% for transbronchial pulmonary biopsies[14] and the prevalence of lung cancer in this study was similar to previous study. Nevertheless the prevalence of lung cancer varied widely across studies, because there were many factors that affected the prevalence of lung cancer such as the experience and expertise of physicians who performed bronchoscopy and patients' factors such as cooperation, comorbidity and facilities of each centers to improve the yield outcome. In this study every patient was performed bronchoscopy by the same physician and were performed bronchoscopy under fluoroscopy. Regional incidence variations directly reflect smoking prevalence. In high smoking prevalence region, the incidence of lung cancer is also highly found.[20] In this study we found the prevalence of lung cancer occurred in male more than female with statical significance which was similar to a previous study.[1] This result may be due to more male patients had smoking history than female patients (79.9 % in male in this study). Smoking was one of the strongest

risk factors for lung cancer in this study. Patients who had smoking history would have 3.7 times risk for lung cancer compared with non smoker. Amount of cigarettes in pack-year was one of risk factors for lung cancer in this study, and patients who had smoking history 10-15 and 20-30 pack-years had statistically significant risk factor, but patients who smoked less than 10 pack-years did not have signifant risk. Although patients who smoked more than 30 pack-years did not have significant risk factor for lung cancer in this study, that maybe because the number of population was quite low in this group.

In previous studies tumor in upper lobes was high probability for lung cancer [11-12], but tumor location was not significant risk for lung cancer in this study. Tumor size more than 7 cms. was significant risk for lung cancer in this study which related to previous study, and the probability of lung cancer was increased with tumor size.[11-12] We found NSCLC more than SCLC (83.7% for NSCLC and 11.6% for SCLC) in this study which related to reviewed literature.[5] From a previous study there was NSCLC about 85% and SCLC about 15% of all lung cancers. The most histological type of lung cancer found in this study was adenocacinoma (51.2%) which was similar to Western countries in which adenocarcinoma currently account for over 40% of all lung cancer cases and the fraction of squamous cell carcinoma decreased from about 30% to 20% due to the significant reductions of smoking during the last fifty years.[21]

In this study there were other causes for lung nodules or lung masses beyond lung cancer from histological type. There were granuloma, chronic inflamation, fibrosis, eosinophillic pneumonia and sarcoma.This finding can help physicians to prove diagnosis of patients who present with lung nodules or lung masses by tissue histology confirmation for definite diagnosis and proper management.

The limitations of this study was some patients in non lung cancer group whose pathology reports showed negative for granoloma or malignancy, might have been lung cancer, but some of them denied further investigation and prefered palliative care treatment, and some patients were lost to follow up and some of them developed brian metastasis without tissue histology to confirm primary lung cancer or metastases.

Most lung cancer patients in this study were stage III and IV (44.7, 39.5% respectively) leading to poor prognostic outcome. In developed countries there were more lung cancer patients in early stage I or II[22] than Thailand, because the higher facilities and using advanced instruments to improve the yield outcome in early detection of lung cancer such as positron emission tomography (PET) in general practice.[23-25] In some countries there were lung cancer screening in high risk groups leading to higher incidence of early stage lung cancer than in Thailand.[26] Previous studies revealed the highest efficacy of lung cancer screening by using low dose computerised tomogragpy (CT) scan, but this has not shown improvement in mortality outcome.[27-29] Cost and effectiveness should be taken into consideration for lung cancer screening in each center.[30]

CONCLUSION

Prevalence of lung cancer of patients who presented with lung nodules or lung masses at the chest clinic of Phrae Hospital was 51.8%. Smoking is a significant risk factor for lung cancer. The basic information from this study might be beneficial to physicians for lung cancer management and performing lung cancer study in the future.

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