Clinical Manifestation and Survival of Patients with Non-Small Cell Lung Cancer

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A retrospective study of clinical manifestations and survival of patients with non-small cell lung cancer (NSCLC) in Sonklanagarind Hospital between 1995-98 was undertaken. There were 209 evaluable NSCLC patients enrolled in the study. NSCLC was common in elderly men who smoked. Major symptoms were cough 74.9%, weight loss 61.6% and dyspnea 54.6%. Chest pain and hemoptysis were presented in only 31.3% and 29.2% respectively. Adenocarcinoma was found in 109 patients (52.1%) , squamous cell carcinoma in 71 patients (34.0%), and large cell carcinoma in 8 patients (3.8%). Only 28 patients (13.4%) were in stage I or II. Surgery was performed in 18 cases (8.6%). Radiation for palliative treatment was used in 74 cases (35.4%). Fifty-four patients (25.8%) received chemotherapy. Forty-two patients received mitomycin, vinblastine and cisplatin regimen (MVP). The response to treatment comprised 3 cases (7.1%) with complete response, and 9 cases (21.4%) with partial response. The survival of the patients in stages I and II was lower than reported from Western countries but in stages III and IV the survival was comparable. Chemotherapy tended to improve survival in advanced stage NSCLC.

Keywords : *Non-small cell lung cancer, Treatment, Prognosis*

J Med Assoc Thai 2004; 87(5): 503-7

Lung cancer is the most common cancer worldwide and the most common cause of cancer death. In Thailand, data on the incidence of cancer between 1988-1991 showed that lung cancer was the second leading cancer in males and the fourth in females[1]. The most common cancer in males is hepatocarcinoma which is very endemic in the North-East of Thailand. Except in the North-East of Thailand, lung cancer is the most common cancer in males. The report of lung cancer in Songkhla province from the Cancer Registry of Prince of Songkla University in 1996 shows that lung cancer is the most common cancer in males and the sixth in females. Non-small cell lung cancer (NSCLC), which includes the histological subform squamous cell carcinoma, adenocarcinoma, and large-cell carcinoma, comprises 75-80% of all lung cancers. In recent years, the predominant histologic type of lung carcinoma has shifted from squamous cell carcinoma to adenocarcinoma. It is believed that this trend is secondary to the switch by many smokers from high tar, filterless cigarettes to low tar, filtered cigarettes[2].

There is little information on the clinical manifestations and survival of patients with NSCLC in Thailand. This retrospective study was performed to investigate the clinical manifestation, diagnostic investigation, treatment and survival of patients with NSCLC.

Material and Method

Eligibility

The patients in Songklanagarind Hospital included in this study were identified through the database maintained by the Cancer Registry of Prince of Songkla University between January 1, 1995 and December 31, 1998. Patient selection was restricted to cases with histologically proven NSCLC, adequate medical records for clinical history and well documented date of death.

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Patient evaluation

The medical records were reviewed for clinical history, chest roentgenopraphic findings, and diagnostic investigations. Choice of therapy was based on the initial intention to treat. The stage of disease at presentation was based on the TNM classification of lung carcinoma according to the American Joint Committee on Cancer[3]. Clinical response to chemotherapy treatment was based on World Health Organization (WHO) criteria[4]. Measurement of tumor size used chest x-ray or CT scan after 2 courses of chemotherapy. Overall survival time was defined as the time between the date of diagnosis and the date of death. Date of death was collected from the medical records in case of death occuring in hospital or death certificate in case of deaths occurring at home.

Statistical Analysis

The Kaplan Meier method was used to calculate survival which was reported as 1-year, 2-year survival and median survival time. The log-rank test was employed to compare the survival of different groups[5]. A value of $p < 0.05$ was considered statistically significant.

Results

There were 209 evaluable cases of NSCLC during the study period. One hundred and fifty-six (74.6%) were men and 53 (25.4) were women. The characteristics of the patients are listed in Table 1. The age of these 209 patients ranged from 29-99 years with a mean age of 59.1 years (standard deviation = 12.5 years). One hundred and twenty-nine of the 147 males (96.3%) and 5 of the 50 females (10%) were smokers. The histology was adenocarcinoma 52.1%, squamous cell carcinoma 34%, large cell carcinoma 3.8%, mixed adenosqumous 1.4%, neuroendocrine 0.5%, and unclassified NSCLC 8.1%. Seventeen patients (8.1%) presented with stage I disease, 11 (5.3%) with stage II disease, 90 (43.1%) with stage IIIa or IIIb disease, 76 (36.4%) presented with stage IV disease, and 15 (7.2%) with unclassified stage of disease.

Major symptoms related to cancer were cough 74.9%, weight loss 61.6% and dyspnea 54.6%. Chest pain and hemoptysis were presented in only 31.3% and 29.2% respectively. Abnormal chest roentgenography showed a mass lesion in 131 cases (69%), infiltrative lesion in 64 cases (38.6%), and pleural effusion in 55 cases (29.4%). Common sites of lesion were both upper lobes, 39.2% in the right upper lobe and 38.7% in the left upper lobe (Table 2).

Eighteen patients underwent surgery and 15 cases (83.3%) were complete resection. In unresectable cases, 9 cases received chemotherapy and 7 cases received radiotherapy. Radiotherapy was commonly used for palliative management of symptoms due to tumor compression, pain, SVC obstruction, and hemoptysis. Chemotherapy was used in 54 cases (25.8%). Twenty-five cases (46.3%) received combined treatment. Ninety-five patients (46.3%) received best supportive care (Table 3). The most commonly used chemotherapy regimen was mitomycin plus vinblastine plus cisplatin (MVP) and the second was

Table 1. Demographic data of the 209 patients with NSCLC

	N = 209
Mean age SD [range] (years)	59.1 12.5 [29-99]
Sex (%)	
Male	156 (74.6)
Female	53 (25.4)
Smoking (%)	
Male	129/147 (87.8)
Female	5/50 (10.0)*
Cell type (%)	
Adenocarcinoma	109 (52.2)
Squamous cell CA	71 (34.0)
Large cell CA	8 (3.8)
Mixed type	3 (1.4)
Neuroendocrine	1 (0.5)
Unclassified NSCLC	17 (8.1)
Stage	
I	17 (8.1)
II	11 (5.3)
IIIa or IIIb	90 (43.0)
IV	76 (36.4)
Unclassified	15 (7.2)

*P = 0.002

Table 2. Abnormal chest roentgenography

	N (%)
Mass	131(69.0)
Infiltration	64 (38.6)
Effusion	55 (29.4)
Site	
Right upper lobe	60 (39.2)
Right middle lobe	27 (19.2)
Right lower lobe	49 (32.3)
Left upper lobe	58 (38.7)
Left lower lobe	40 (29.2)

paclitaxel plus carboplatin (PC). Forty-two patients received MVP regimen. The response to treatment comprised 3 cases (7.1%) with complete response, and 9 cases (21.4%) with partial response. Fifteen cases (35.8%) were stable or progressive diseases (Table 4). Twelve cases received other chemotherapy regimens.

Table 5 summarizes the survival data of the 209 patients with NSCLC stage I-IV. One-year and 2-year survival and median survival time of stage I were 58.8%, 41.2% and 58 weeks, respectively. Survival of stage II was 45.5%, 45.5% and 26 weeks, of stage III 34.4%, 23.3% and 32 weeks, and of stage IV was 38.2%, 25.0% and 26 weeks, respectively. The cumulative survival of stage I, II, III, and IV is shown in Fig. 1. Median survival and one-year survival of stage III and IV were more favorable in the chemotherapy group using MVP regimen compared with the supportive treatment group (33 weeks vs. 21 weeks and 41.0 vs.32.5%) but this difference was not statistically significant. Fig. 2 shows the survival curves of stage III and IV patients who received chemotherapy, MVP regimen, compared to non-chemotherapy patients.

Table 3. Management of lung cancer

Treatment	N (%)
Surgery	18 (8.6)
Resectable	15
Unresectable	3
Radiation	74 (35.4)
Radiation alone	51
Combined treatment	23
Chemotherapy	54 (25.8)
Chemotherapy alone	29
Combined treatment	25
Supportive treatment	95 (45.5)

Table 4. The results of chemotherapy

	No (%)
Total cases	42
Mean courses of chemotherapy SD	2.64 1.86
Response	
Complete response (CR)	3 (7.1)
Partial response (PR)	9 (21.4)
Total response (CR + PR)	12 (28.6)
Stable	7 (16.7)
Progression	8 (19.1)
Not evaluable	15 (35.7)

Table 5. Survival data of the 209 patient with NSCLC

Stage	No	1-year survival (%)	2-year survival (%)	Median survival (week)
I	17	58.8	41.2	58
II	11	45.5	45.5	26
III	90	34.4	23.3	32
IV	76	38.2	25.0	26
III+IV received MVP regimen	39	41.0	23.1	33
III+IV without chemotherapy	117	32.5	24.8	21*

* NS for the comparison with stage III + IV received MVP regimen

Discussion

The present study confirms that NSCLC is associated with smoking males. Unlike the previous reports of Chulalongkorn University Hospital[6] and Lampang Hospital[7], the histologic type of lung

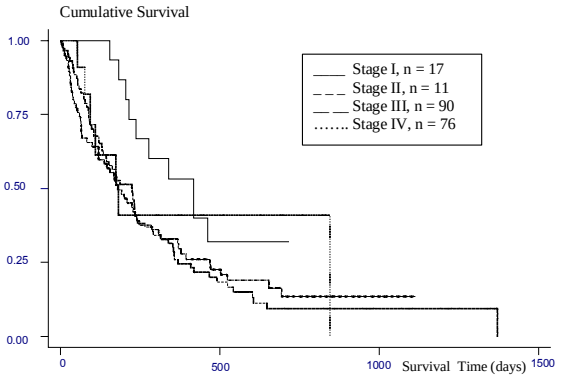

Fig. 1 A comparison of survival of NSCLC stage I, II, III, and IV

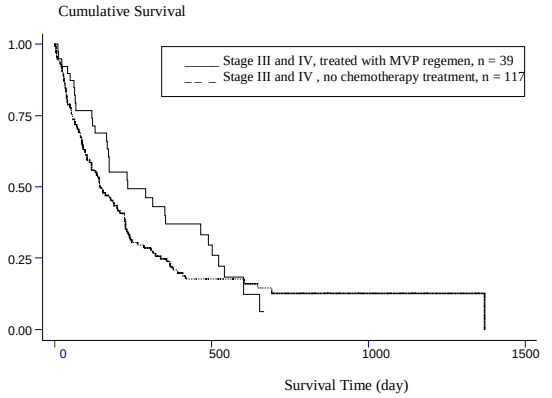

Fig. 2 A comparison of survival of stage III and IV patients treated with MVP regimen and without chemotherapy

carcinoma was predominately adenocarcinoma (52%), not squamous cell carcinoma. In recent years, the predominant histologic type of lung carcinoma has shifted from squamous cell carcinoma to adenocarcinoma[8]. It is believed that this trend is secondary to the switch by many smokers from high tar, filterless cigarettes to low tar, filtered cigarettes[2]. Data from Western countries showed that 20-35% of cases are operable[9,10] . Most of the patients in this study presented with advanced stage of disease, and only 28 patients (13.4%) presented with stage I and II disease. This result is compatible with other studies in Thailand. The resectable cases in Siriraj Hospital comprised 11%[11,12], and stage I and II in Srinagarind Hospital only 5%[13]. NSCLC is potentially curable only in stages I and II. There is no effective screening method for lung cancer at the present time. Physicians should investigate for lung cancer in a high risk patient presenting with non specific chest symptoms. The common sites of lung cancer are both upper lobes and pleural effusion is found in about one-third of patients. Radiotherapy was commonly used (35%) for palliative therapy. About twenty-five percent of patients received chemotherapy, most usually MVP regimen. The result of MVP in the present study (overall response 29%) is comparable to that in the study by ECOG[14]. Randomized trials reported by ECOG before the study of a new generation of chemotherapy such as paclitaxel, gemcitabine, etc showed that phase III combination chemotherapy produced response rates of no more than 30%.

The staging in the present study did not classify stage I and II to subgroups Ia, Ib, IIa, and IIb owing to the small number of patients. The 1-year and 2-year survival of stage I in the present study were 59% and 41% which is very low compared to 72% and 54% of stage Ib reported by Mountain[3]. Stage II had a 1-year survival of 46% which is low compared to 59% of stage IIb reported by Mountain[3]. The stage I and II in the present study may be understaged, resulting in bad prognosis in these groups. The 1-year and 2-year survival of stages III and IV in the present study are comparable to previous reports. Over the past 15 to 20 years a small but significant improvement has been seen in the treatment of patients with advanced or metastatic non-small cell lung cancer. By the late 1980s the median survival had increased from approximately 4 months in untreated patients to approximately 7 to 8 months with traditional cisplatin-based chemotherapy combinations[15]. The median survival in advanced stage and metastatic disease in the present study was 27 weeks. Median survival was more favorable for the chemotherapy group, MVP regimen, compared with the supportive treatment group (33 weeks vs. 21 weeks). Riantawan et al[16] reported the median survival in advanced stage and metastatic disease to be only 11 weeks in the Central Chest Hospital. Aims of treatment of advanced stage lung cancer are increased response rate, increased survival, improved quality of life, and cost effectiveness. The quality of life of patients could not be assessed in the present retrospective study. MVP regimen should be considered in the treatment of advanced stage lung cancer because of the modest response, slight increased survival and low expense.

Conclusion

The clinical characteristics of 209 patients with NSCLC were reported. Most of the patients presented in the inoperable stage. Survival in stage I and II disease was lower than in other reports but that of stage III and IV disease was comparable. Radiotherapy was commonly used for palliative treatment. Chemotherapy was used in one-fourth of the patients. The response to chemotherapy was about 29% and median survival may be better than in patients without chemotherapy.

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อาการทางคลินิก และการพยากรณ์โรคในผู้ป่วยมะเร็งปอดชนิด non-small cell lung cancer

กรีฑา ธรรมคำภีร์

ได้ศึกษาย้อนหลังผู้ป่วยมะเร็งปอดชนิด non-small cell lung cancer (NSCLC) ที่โรงพยาบาลสงขลานครินทร์ ระหว่างปีพ.ศ. 2538 ถึงปี พ.ศ. 2541 จำนวน 209 ราย พบว่าผู้ป่วยส่วนมากเป็นผู้ชายสูงอายุและสูบบุหรี่ อาการสำคัญที่พบคือไอร้อยละ 74.9 น้ำหนักลดร้อยละ 61.6 หอบเหนื่อยร้อยละ 54.6 มีอาการเจ็บหน้าอก และไอเพียงร้อยละ 31.3 และ 29.2 ตามลำดับ ชนิดของเซลล์ที่พบบ่อยที่สุดคือ adenocarcinoma 109 ราย (52.1%) เป็น squamous cell carcinoma 71 ราย (34.0%) เป็น large cell carcinoma 8 ราย (3.6%) มีผู้ป่วยระยะที่ 1 และ 2 จำนวน 28 ราย (13.4%) ได้รับการผ่าตัด 18 ราย (8.6%) ผู้ป่วยได้รับการฉายแสง 74 ราย (35.4%) ได้รับการรักษาด้วยเคมีบำบัด 54 ราย (25.8%) ผู้ป่วยที่ได้รับเคมีบำบัดสูตร mitomycin, vinblastine และ cisplatin regimen (MVP) 42 ราย ผลการรักษาได้เป็น complete response 3 ราย (7.1%) และ partial response 9 ราย (21.4%) การพยากรณ์โรคของผู้ป่วยระยะที่ 1 และ 2 ต่ำกว่ารายงานจากต่างประเทศแต่ผู้ป่วยระยะที่ 3 และ 4 มีการพยากรณ์โรคไม่แตกต่างกัน ผลการรักษาด้วยยาเคมีบำบัดในผู้ป่วยระยะลุกลามมีแนวโน้มว่าจะช่วยให้การพยากรณ์โรคดีขึ้น