

มะเร็งปอดชนิดเซลล์ไม่เล็กในโรงพยาบาลศรีนครินทร์: 2543-2553, ทะเบียนมะเร็งโรงพยาบาล

วิยะดา ปัญจรัก^{1,4}, กฤติกา สุวรรณรุ่งเรือง², โกสินทร์ วิระษ^{3,4*}

¹ภาควิชาสรีรวิทยา, คณะแพทยศาสตร์, มหาวิทยาลัยขอนแก่น

²หน่วยมะเร็ง, โรงพยาบาลศรีนครินทร์

³ภาควิชาอายุรศาสตร์, มหาวิทยาลัยขอนแก่น, กลุ่มวิจัยมะเร็งแบบองค์รวม

⁴มหาวิทยาลัยขอนแก่น, กลุ่มวิจัยมะเร็งแบบองค์รวม

Non-small Cell Lung Cancer (NSCLC) in Srinagarind Hospital: 2000-2010, Hospital Based

Wiyada Punjaruk^{1,4}, Krittika Suwanrungruag², Kosin Wirasorn^{3,4*}

¹Department of Physiology, Faculty of Medicine, Khon Kaen University

²Cancer Unit, Srinagarind Hospital

³Division of Oncology, Department of Medicine

⁴Khon Kaen University, Comprehensive Cancer Research Group (KKU CCRG)

หลักการและวัตถุประสงค์: มะเร็งปอดเป็นมะเร็งที่พบบ่อยทั่วโลก โดยเฉพาะมะเร็งปอดชนิดเซลล์ไม่เล็ก และเป็นสาเหตุการเสียชีวิตในประเทศต่าง ๆ วัตถุประสงค์ของการศึกษาคือ เพื่อทบทวนลักษณะทางคลินิกของผู้ป่วยมะเร็งปอดชนิดเซลล์ไม่เล็กในโรงพยาบาลศรีนครินทร์ ระหว่างปี พ.ศ. 2543-2553 และวิเคราะห์ระยะเวลาการรอดชีวิตของผู้ป่วยโรคมะเร็งดังกล่าว

วิธีการศึกษา: ทำการศึกษาในผู้ป่วยมะเร็งปอดชนิดเซลล์ไม่เล็กรายใหม่ที่ได้ลงทะเบียนในโรงพยาบาลศรีนครินทร์ ระหว่างวันที่ 1 มกราคม 2543 ถึงวันที่ 31 ธันวาคม 2553 ข้อมูลที่นำมาศึกษาจากระบบการลงทะเบียนผู้ป่วยมะเร็งของจังหวัดขอนแก่น ลักษณะทางคลินิกของผู้ป่วยและระยะเวลาการรอดชีวิตได้ถูกนำมาวิเคราะห์ทางสถิติ

ผลการศึกษา: จำนวนผู้ป่วยรายใหม่ของมะเร็งชนิดเซลล์ไม่เล็กในระหว่างปี พ.ศ. 2543-2553 ในโรงพยาบาลศรีนครินทร์มีแนวโน้มคงที่ทั้งเพศชายและหญิง จำนวนผู้ป่วยเพศชายสูงกว่าหญิงประมาณสองเท่าตลอดระยะเวลาของการศึกษาสัดส่วนของผู้ป่วยมะเร็งปอดชนิดเซลล์ไม่เล็กต่อผู้ป่วยโรคมะเร็งรายใหม่ทั้งหมดเป็น 1: 11.91 (4,176 of

Background and Objectives: Lung cancer is the most common cancer occurred worldwide especially non-small cell lung cancer (NSCLC) and it is the leading cause of death in many countries. The aim of this study is to review the characteristics of NSCLC patients who received treatment in Srinagarind Hospital during 2000-2010. Additionally, survival time was also presented in this study.

Methods: All new NSCLC cancer cases registered in Srinagarind Hospital between January 1st, 2000 and December 31st, 2010 were included in this study. Our data were obtained from the Khon Kaen Cancer Registry. The characteristics of patients and survival time were analysed.

Results: The number of new NSCLC cases studied during 2000-2010 in Srinagarind Hospital was fairly constant in both male and female NSCLC patients. Numbers of NSCLC male cases were approximately 2 folds higher than female cases throughout the study

*Corresponding author:

Kosin Wirasorn, Department of Medicine, Faculty of Medicine, Khon Kaen University

E-mail : wkosin@kku.ac.th

49,763 ราย) หรือ ร้อยละ 8.39 พบว่าสัดส่วนผู้ป่วยเพศชาย สูงกว่าหญิง คิดเป็น 2.57:1 ค่ามัธยฐานของอายุผู้ป่วย คือ 60 ปีในเพศชายและ 57 ปี ในเพศหญิง ครึ่งหนึ่งของผู้ป่วย จำนวนทั้งหมดมาพบแพทย์ในระยะที่ 4 ส่วนระยะที่ 3 พบมากเป็นอันดับสอง ระยะเวลาการรอดชีวิตของผู้ป่วย โดยรวม คือ 7.92 เดือน (ช่วงความเชื่อมั่น ร้อยละ 95, 7.42, 8.52; $p < 0.05$) นอกจากนี้ ระยะเวลาการรอดชีวิตโดยรวมของผู้ป่วยในระยะที่ 1-4 คือ 39.72, 21.84, 11.26 และ 6.24 เดือน ตามลำดับ

สรุป: แนวโน้มจำนวนผู้ป่วยรายใหม่ของมะเร็งปอดชนิด เซลล์ไม่เล็กมีจำนวนเพิ่มขึ้นอย่างต่อเนื่อง ซึ่งผู้ป่วยส่วนมาก มาพบแพทย์ด้วยระยะลุกลามของโรคส่งผลให้ระยะเวลา การรอดชีวิตของผู้ป่วยสั้นลง

คำสำคัญ: มะเร็งปอดชนิดเซลล์ไม่เล็ก, ระยะเวลาการรอดชีวิต, โรงพยาบาลศรีนครินทร์

period. The ratio of new NSCLC cases per total cancer cases was 1:11.91 (4,176 of 49,763 cases) or 8.39%. NSCLC was found in male at a higher frequency compared to female (2.57:1). The mean age at primary diagnosis of NSCLC was 60 years in male and 57 years in female. Half of NSCLC patients commonly presented with stage IV and stage III of disease was secondly found (19.76%). Overall median survival time of all NSCLC patients was 7.92 months (95% confidence interval (CI), 7.42, 8.58; p value < 0.05). Additionally, the overall median survival times of patients with stage I-IV were 39.72, 21.84, 11.26, and 6.24 months, respectively.

Conclusions: The trends of NSCLC are accelerating increasing and NSCLC patients usually presented with advanced stages of diseases resulting in poor survival rate.

Key words: non-small cell lung cancer, survival, Srinagarind hospital

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Introduction

Lung cancer is the most common cancer occurring worldwide and it is the leading cause of death in many countries¹. Cigarette smoking is an important factor leading to lung cancer². Lung cancer is classified into 2 types based on the histopathologic characteristics; small cell lung cancer (SCLC) and non-small cell lung cancer (NSCLC). NSCLC is the most common type of lung cancer. The most common subtype of NSCLC is adenocarcinoma³. Lung cancer patients usually present with chronic cough, hemoptysis and body weight loss. American Joint Committee on Cancer (AJCC)/International Union Against Cancer (UICC) staging system classifies lung cancer based on TNM staging system⁴. Basically, the important factors used to evaluate the staging of NSCLC are sizes and extension of tumor (T), regional lymph node involvement (N) and distant metastasis (M). These 3 factors (T, N and M) are essential for determining the staging of disease. Four stages of lung cancer are defined based on this classification system, stage I-IV. Small tumor size of lung cancer located within the lung is classified as

stage I. If hilar lymph node involvement is detected, this is defined as stage II. The stage III is lung cancer patients presenting with mediastinal lymph node metastasis. When lung cancer distantly spreads to contralateral lung, pleura, brain, bone and adrenal glands, this is classified as stage IV.

The optimal treatment of choice for NSCLC depends on both the stages of disease and patient performance status⁵. Hence, the standard treatment for the early stage of lung cancer (stage I) is single treatment, surgery, which is effectively adequate for this stage. For stage II of lung cancer, patients should receive adjuvant chemotherapy after surgery performed. The multi-modalities of treatment especially concurrent chemo-radiation are applied for lung cancer patients with stage III. The principal treatment for stage IV lung cancer patients is systemic treatment such as chemotherapy or molecular targeted therapy.

Srinagarind hospital is a tertiary health care center covering patients in the Northeast (NE) Thailand. This hospital receives referred cases with advanced and

complicated conditions highly leading to morbidity and mortality from all over the region. Additionally, Srinagarind hospital provides health service for approximately 22 million people within the NE. Malignant diseases are advanced and complicated conditions which require the tertiary health care center for the most appropriate treatment. In addition, Srinagarind hospital is a health care center comprising many subspecialty physicians expertising on malignancy, hence, most cancer cases in the NE are referred to Srinagarind hospital to receive the proper management. Therefore, various types of cancers including NSCLC are coming to Srinagarind hospital and the cancer situation occurring in Srinagarind hospital might reflect the situation of cancer in NE as a whole.

The aim of this study is to review the characteristics of NSCLC patients who received specific treatment in Srinagarind hospital during 2000-2010. Additionally, survival time of patients with different stages was analysed and presented in this study.

Materials and methods

Case definition:

All new NSCLC cancer cases registered in Srinagarind Hospital from January 1st, 2000 and December 31st, 2010 were included in this study. This study is officially approved by the Khon Kaen University Ethics Committee for Human Research based on the Declaration of Helsinki and the ICH Good Clinical Practice Guidelines with HE571238 of reference number.

Sources of data:

Srinagarind hospital, Khon Kaen University (a thousand-bed university hospital), Khon Kaen, Thailand, is situated in the center of NE Thailand and accepts all referred cases from other health care centers in this region. Our data were obtained from the Khon Kaen Cancer Registry which has recorded data of all cancer cases treated in this hospital since 1987. All data were verified, checked for coding duplication and entered into the CANREG software (Version 4, available from <http://www.iacr.com.fr/canreg4.htm>). The data are normally collected from each cancer patient including age, sex,

date of birth, date of diagnosis, method of diagnosis, primary site of cancer, extension or metastasis, histology of cancer, date of last visit, vital status at last follow-up and other necessary information. However, only relevant data were presented in this study.

Statistical analysis

The survival time was defined since the date of diagnosis to the date of last follow up or death from any causes. The data were analysed using Poisson regression to determine the trends of new case number throughout the study period. Patients' characteristics were presented as mean and percentage. The cumulative survival rate is presented by the Kaplan Meier curve. Comparison of the median survival based on the stages of disease was analysed using Log-rank test. The statistical analyses were performed using statistical program R, version 3.1.1 (<http://www.R-project.org/>). A p-value less than 0.05 was considered statistical significance. The study was complete for analysis in June 2014.

Results

The number of new NSCLC cases studied during 2000-2010 in Srinagarind Hospital was fairly constant in both male and female NSCLC patients (Figure 1). The overall increment of new NSCLC cases was only 1% throughout the study period. Such new cases of male had approximately 2 folds higher than female cases throughout the study period.

The characteristics of patients are presented in Tables 1. The ratio of new lung cancer cases per total cancer cases is 1: 11.91 (4,176 of 49,763 cases) or 8.39%. Lung cancer was occurred in male at a higher frequency compared to female (2.57:1). The mean age at primary diagnosis of lung cancer was 60 years in male and 57 years in female. Almost half of patients with lung cancer (42.17%) was confirmed the final diagnosis from the evidence of pathological findings and more than 1/3 of lung cancer patients were undergone endoscopy and radiology for the final diagnosis. Half of lung cancer patients commonly presented with stage IV and stage III of disease was secondly found in lung

cancer patients. Non-regional lymph nodes and bone were the most common metastatic sites for lung cancer. Only 2,695 (64.5%) of lung cancer patients received specific treatment in Srinagarind Hospital. Both chemotherapy and radiotherapy were the standard treatment modalities in these patients.

Overall median survival time of all lung cancer patients was 7.92 months (7.42-8.58 months) shown in Figure 2. The overall median survival times of patients with stage I-IV were 39.72, 21.84, 11.26, and 6.24 months, respectively. Certainly, patients with stage I of disease had fairly better survival rate than other stages and the late stage (stage IV) of lung cancer had the worse survival time.

Table 1 General demographic data of lung cancer patients in Srinagarind Hospital, 2000-2010

Variables	Number (%)
Sex = male: female	3,008:1,168 Male: 72% Female: 28%
Age (yr): Mean (SD)	Male: 60.3 (11.3) Female: 57.6 (11.8)
Basis of diagnosis	Clinical = 0.36% Endoscopy & Radiology = 35.06% Surgery without histology = 0.55% Specific biochem/Immuno test = 0.41% Cytology = 14.61% Histology of Metastasis = 6.85% Histology of primary = 42.17%
Staging	stage 1 = 2.16% stage 2 = 2.71% stage 3 = 19.76% stage 4 = 50.17% NA = 25.22%
Metastatic sites	lymph nodes: 22.77% bone: 20.97% liver: 9.14% lung or pleura: 10.83% brain: 18.05% peritoneum: 0.76% others: 10.77% multiple: 6.7%
Treatment	Surgery: 23.4% Chemotherapy: 38.6% Radiation: 38.0%

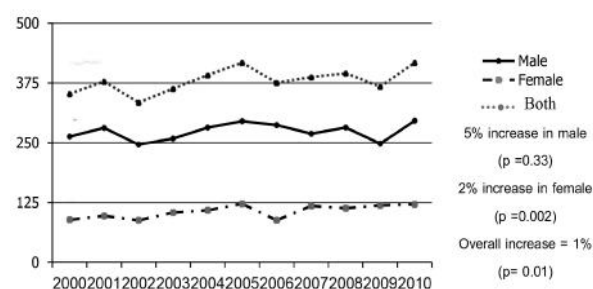


Figure 1 Trends of new NSCLC cases in Srinagarind Hospital during 2000-2010

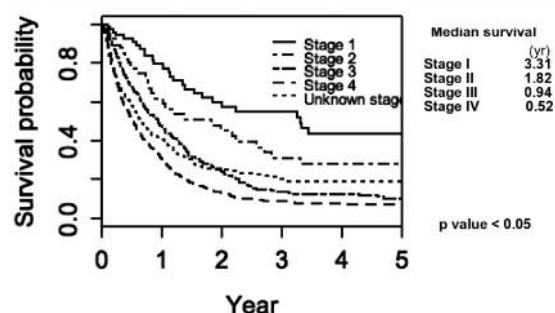


Figure 2 The overall survival rate of lung cancer patients with different stages of disease in Srinagarind Hospital during 2000-2010.

Discussion

This study revealed that NSCLC was found at higher frequency compared to the previous decade and it gradually increases^{6,7}. Such high frequency found in Srinagarind Hospital during the recent decade is possibly because greatly improved the medical technology relating to advanced imaging system for early diagnosis in the hospital. Additionally, the health care service is continually improved to get high quality of medical service and all patients easily reach the tertiary health care service to receive accurate diagnosis and the standard treatment. Currently, the health information is easily accessed, therefore, patients have more awareness of their health problems resulting in early coming for diagnosis. Interestingly, the incidence of lung cancer in female was found at higher frequency compared to the past history of female lung cancer during the last decade. This possibly results from the genetic changes and *Epidermal Growth Factor Receptor (EGFR)* mutation. Mutation of EGFR is recently

found at high frequency in female and it is the key factor, which causes lung cancer in non-smoking patients. Additionally, the effective campaign of stop smoking in Thailand influences on decreasing number of new male smokers. However, the number of new lung cancer cases in male was still found at higher proportion compared to female. Consistently, the report studied in the Western countries stated that high frequency of lung cancer cases were detected in male⁸. The majority of lung cancer cases frequently presented with the advanced stages of disease having distant metastasis, which is consistent with the previous studies⁹. Distant metastasis of lung cancer was commonly presented in lymph node and bone, which is similar to the previous^{10,11}. Both sites of distant metastasis are the common feature of adenocarcinoma subtype. Presently, cancer screening test for lung cancer is still ineffective and this cancer is not recognised as problematic issues. Consequently, the national policy about lung cancer screening is not concerned. Actually, low dose CT scanning of lung is the most effective screening investigation for lung cancer. However, chest x-ray is still routinely performed for annual check¹up for lung screening test. Hence, the early stage of lung cancer in patients is impossibly detected using chest x-ray. Consequently, most of lung cancer patients always presented with stage IV of disease¹². Additionally, the average survival time of lung cancer patients studied in Srinagarind Hospital was comparable with the survival time found in lung cancer patients with stage IV of disease. In addition, the survival time analysed was lower than the previous studies¹³. This is possibly because some lung cancer patients received the best supportive treatment without the standard treatment. Additionally, chemotherapeutic regimen used in these patients is cisplatin and etoposide, which are the second generation of chemotherapy for NSCLC. Hence, this possibly leads to lower survival time compared to the studies using the third generation of chemotherapy such as placitaxel and carboplatin or the combination of cisplatin and gemcitabine¹⁴.

Advantages and limitations of this study

The advantages of this study are that this study presents the overview of lung cancer in the NE Thailand. This information is able to provide significant data for the government to concern about the prevention of CA lung and the early detection of CA lung. The limitation of this study is that study is the retrospective study. Therefore, recorded data are not complete in aspects of percentage of weight loss in patients and the metastatic sites. Additionally, half of population included in this study was stage IV patients. Hence, the results found in this study might represent the situation of stage IV lung cancer rather than lung cancer patient with all stages.

Conclusion

The trends of NSCLC are accelerated increasing especially in female and lung cancer patients usually presented with advanced stages of diseases resulting to poor survival rate. If abnormal symptoms of lung cancer are able to be recognised, the definite diagnosis can be confirmed at the early stage of disease. This will be a very important prognostic factor for patients in anticipating the survival time. The results provide important data for the government to have a policy for lung cancer screening.

References

1. Siegel R, Naishadham D, Jemal A. Cancer statistics, 2013. *CA Cancer J Clin.* January 2013; 63: 11–30.
2. Gomez Raposo C, De Castro Carpeno J, Gonzalez Baran M. [Causes of lung cancer: smoking, environmental tobacco smoke exposure, occupational and environmental exposures and genetic predisposition]. *Med Clinca* 2007; 128: 390–6.
3. Oyewumi MO, Alazizi A, Wehrung D, Manochakian R, Safadi FF. Emerging Lung Cancer Therapeutic Targets Based on the Pathogenesis of Bone Metastases. *Int J Cell Biol* [internet]. 2014 [referred to 14 September 2014]; 2014. Searched from: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4147348/>

4. Tsim S, O'Dowd CA, Milroy R, Davidson S. Staging of non-small cell lung cancer (NSCLC): a review. *Respir Med* 2010; 104: 1767–74.
5. Goldstraw P, Ball D, Jett JR, Le Chevalier T, Lim E, Nicholson AG et al. Non-small-cell lung cancer. *Lancet* 2011; 378(9804): 1727–40.
6. Vatanasapt V, Martin N, Sriplung H, Chindavijak K, Sontipong S, Sriamporn H et al. Cancer incidence in Thailand, 1988–1991. *Cancer Epidemiol Biomark Prev Publ Am Assoc Cancer Res Cosponsored Am Soc Prev Oncol* 1995; 4: 475–83.
7. Sriplung H, Sontipong S, Martin N, Wiangnon S, Vootiprux V, Cheirsilpa A et al. Cancer incidence in Thailand, 1995–1997. *Asian Pac J Cancer Prev* 2005; 6: 276–81.
8. Alberg AJ, Ford JG, Samet JM, American College of Chest Physicians. Epidemiology of lung cancer: ACCP evidence-based clinical practice guidelines (2nd edition). *Chest* 2007; 132 (3 Suppl): 29S – 55S.
9. Klarod K, Hongsprabhas P, Khampitak T, Wirasorn K, Kiertiburanakul S, Tangrassameeprasert R, et al. Serum antioxidant levels and nutritional status in early and advanced stage lung cancer patients. *Nutr Burbank Los Angel Cty Calif* 2011; 27 (11-12): 1156–60.
10. Sakao Y, Miyamoto H, Yamazaki A, Oh T, Fukai R, Shiomi KA, et al. Prognostic significance of metastasis to the highest mediastinal lymph node in nonsmall cell lung cancer. *Ann Thorac Surg* 2006; 81 (1): 292–7.
11. Rossi A, Gridelli C, Ricciardi S, de Marinis F. Bone metastases and non-small cell lung cancer: from bisphosphonates to targeted therapy. *Curr Med Chem* 2012; 19: 5524–35.
12. Haws L, Haws BT. Aerodigestive cancers: lung cancer. *FP Essent* 2014; 424: 32–47.
13. Riihimäki M, Hemminki A, Fallah M, Thomsen H, Sundquist K, Sundquist J, et al. Metastatic sites and survival in lung cancer. *Lung Cancer Amst Neth* 2014; 86: 78–84.
14. Ramalingam S, Belani C. Systemic Chemotherapy for Advanced Non-Small Cell Lung Cancer: Recent Advances and Future Directions. *Oncologist* 2008; 13 (Suppl1): 5–13.

