Survival Analysis of Thai Patients with Non-Small-Cell Lung Cancer Undergoing Surgical Resection

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Abstract

This study examined the survival duration among patients with non-small-cell lung cancer (NSCLC) undergoing surgical resection from January 1988 to December 1992 at the Central Chest Hospital, Thailand. Patients were followed-up until death or survival as of September 1997. Survival durations for different stages were analysed by Kaplan-Meier analysis and log rank test.

A total of 127 patients with histologically proved NSCLC underwent 79 lobectomies, 9 bilobectomies, 39 pneumonectomies during 1988-1992. The mean age was 60 years (SD 10.4). There were 103 males and 24 females. Percentage of histologic types were: 59 per cent adenoCA, 35 per cent squamous cell CA, and 6 per cent large cellCA. Survival analysis was feasible in 88 patients, 38 alive and 50 deaths. 1-yr, 2-yr, and 5-yr survival were as following : 85 per cent, 78 per cent, and 60 per cent in stage 1 (n = 47); 70 per cent, 50 per cent, and 30 per cent in stage 2 (n = 12); and 54 per cent, 23 per cent, and 15 per cent in stage 3a (n = 29) [log rank 19.06, df 2, p = 0.0001]. Based on the present study, the survival outcome in patients with lung cancer beyond stage 1 is uniformly poor. Measures should be made to diagnose early stage disease and expedite surgery in order that a better survival outcome can be achieved.

Key word : Lung Cancer, Surgery, Survival

Despite decades of global efforts, lung cancer remains common and represents a leading cause of cancer-related deaths worldwide[1]. At least three-fourths of patients with lung cancer are unresectable at presentation because the disease is either metastatic or locally advanced[1,2]. Further, survival among those beyond surgical stage is uniformly short[3,4]. Early surgical resection in eligible cases is therefore the most important strategy to reduce mortality from lung cancer.

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Survival duration in patients with lung cancer following resection has been described[5-7]. However, these data originated wholly from developed countries, mainly North America and Europe. Several factors related to survival are clearly modulated by environmental and socio-economic aspects. There are conceivable differences among countries in various geographical locations with different health care systems and referral facilities.

Keeping this in perspective, only the survival data among Thai patients with lung cancer following resection would accurately testify to the surgical benefit among our population. The data obtained will be of immense value. At present, however, such data do not exist.

As the first analysis of this aspect in Thailand, therefore, the present study examines the survival duration among patients with lung cancer undergoing surgical resection.

MATERIAL AND METHOD

The study was conducted at the Central Chest Hospital, Nonthaburi, Thailand. This 500-bed, cardiothoracic centre provides referral services for cardio-respiratory diseases for patients from all parts of the country. It is fully equipped with diagnostic facilities including fibreoptic bronchoscopy, percutaneous needle aspiration/ biopsy, and computed tomography (CT).

Patients and method

It is our policy at the Central Chest Hospital to expedite a definitive diagnosis in patients with suspected lung cancer so as to ensure early resection in cases eligible for surgery, i.e. stage 1, 2, and 3a, based on the new international TNM staging system[8]. Preoperative assessment is made in a standard manner, based on physical evaluation, bronchoscopic findings and pulmonary function testing[9,10]. CT scan of the chest was performed in all cases with proximal tumor, or cases with hilar or mediastinal involvement on chest radiograph.

Patients with small cell lung cancer received cytotoxic chemotherapy or radiation therapy; therefore, they were not involved in the present retrospective analysis.

Details of data collection

From the operative list at the operative theatre and from the histopathologic reports at the division of pathology, the names, gender, age, hospital numbers, and histopathologic types were obtained on consecutive patients with non-small-cell lung cancer (NSCLC) undergoing surgical resection from January 1988 - December 1992. The medical records were then traced from the division of medical records. The records were systematically reviewed. The bronchoscopic details, CT scan data, operative findings, full pathologic reports including the presence of metastases to resected lymph nodes and the clearance of resection margin were collated. Radical clearance of all mediastinal lymph nodes was not routinely undertaken, however, it is our practice to resect all abnormal looking nodes and routinely to sample nodes immediately proximal to the resection margin.

The date of death was documented. For the purposes of the present study, survival was defined as "the timespan from the date of operation to the date of death". Data from patients who died within 28 days after thoracotomy were excluded from the survival analysis as these data more likely reflect peri-operative complications. Survival duration was calculated as of September 1997.

Sources of survival data

Regular follow-up is maintained as far as possible in patients undergoing surgery in our hospital. Survival data were thus available in a number of patients with complete follow-up. However, there existed a proportion of patients who, for convenience, opted to seek a long-term follow-up from local health authorities. Predictably therefore, survival data would be absent from the medical records. For these cases, nonetheless, a stamped-addressed envelope to the patient and next-of-kin was sent and they were asked to document in a postal reply in one of the three categories : a) the patient was alive and remained well, b) the patient was alive but suffered from health problems (stated), or c) the patient had passed away with the date/ month/ year of death to be kindly provided.

Statistical methods

Survival data are presented as 1-yr, 2-yr, and 5-yr survival in percentage. Kaplan-Meier survival analysis was used to describe survival and log rank test was employed to evaluate differences in survival among different stages[11,12]. Statistical significance was assessed at 5 per cent level. All data analyses were performed using an SPSS statistical programme.

RESULTS

Demographic data

From 1988 to 1992, a total of 127 patients with NSCLC underwent surgical resection. There were 104 males and 23 females. The mean age was 60 years (SD 10.4, range 26-79 yrs) (Fig. 1). In all, 78 lobectomies, 9 bilobectomies, 39 pneumonectomies, and 1 lobectomy with *en bloc* rib resection were performed.

Histopathologic types

Of the total 127 cases, the histologic types were as follows : 75 adenoCAs (including 16 bronchioloalveolar cell types), 44 squamous cell Cas, and 8 large cell CAs.

Thus the percentages of various types were as follows : 59 per cent adenoCA (including 12 per cent bronchioloalveolar cell CA), 35 per cent squamous cell CA, and 6 per cent large cell CA.

Proportion of data source

Of the total 127 patients, the medical records were absent in 21 cases. Of the available 106 medical records, 2 patients undergoing pneumonectomy died at day 14 and 19 postoperatively due to overwhelming pneumonia and acute severe renal failure and were excluded from the analysis. Of the remaining 104 medical records, there were 51 patients with complete follow-up at the Central Chest Hospital until death or survival as of september 1997. There were 29 deaths and 22 patients remained alive. A postal questionnaire was therefore employed in the remaining 53 cases. There were 37 cases who replied, yielding a 70 per cent response rate. Based on the response, 21 cases were dead and 16 cases remained alive. The mail was returned unanswered in view of incorrect address in 6 cases. No information was available in the remaining 10 postal questionnaires.

Total survival analysis was, hence, possible in 88 patients. Forty-seven cases were in stage 1, 12 cases in stage 2, and 29 cases in stage 3a.

Survival outcome

Upon the completion of 5 year follow-up, 38 patients were alive and 50 patients had expired. Fig. 2 illustrates the Kaplan-Meier survival curve among the patients in different stages.

Cumulative survival at 1 year, 2 years, and 5 years were as follows : 85 per cent, 78 per cent, and 60 per cent in stage 1 (n = 47); 70 per cent, 50 per cent, and 30 per cent in stage 2 (n = 12); and 54

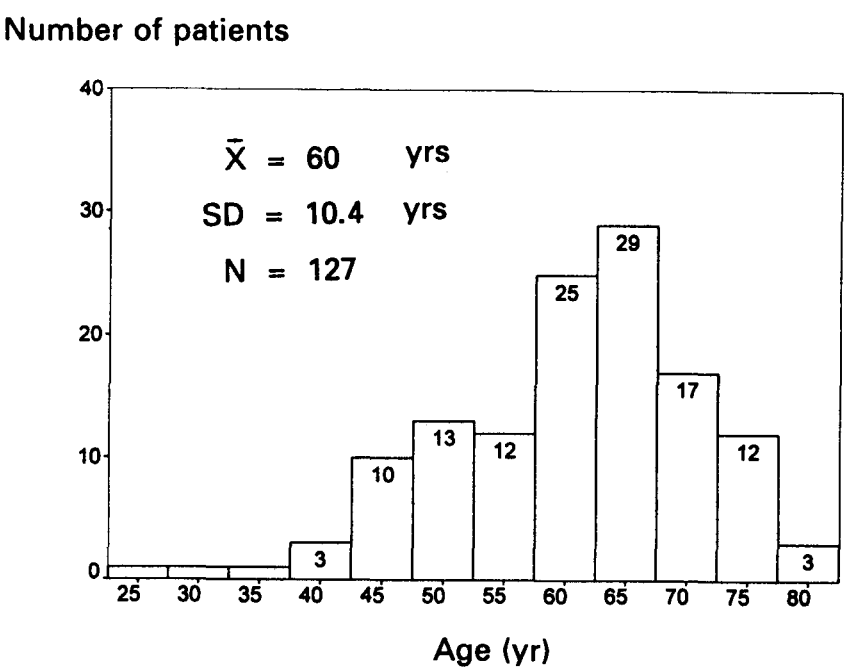

Fig. 1. Histogram showing age group of 127 patients with NSCLC undergoing resection.

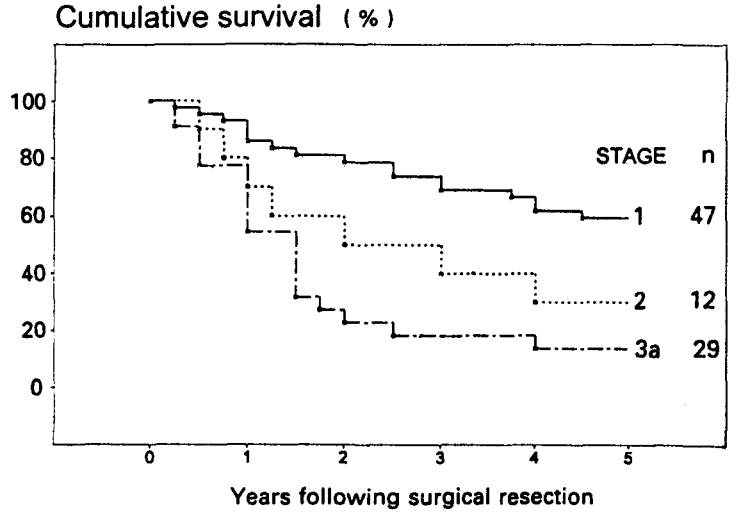

Fig. 2. Kaplan-Meier survival curve in 88 patients with lung cancer following resection.

per cent, 23 per cent, and 15 per cent in stage 3a (n = 29). The differences in survival among different stages were statistically significant (log rank 19.06, df 2, p = 0.0001).

DISCUSSIONS

The present study has systematically described early and long term survival among patients with non-small-cell lung cancer (NSCLC) undergoing surgical resection. Reasonably good survival outcome appears only in stage 1 disease with 85 per cent of the patients surviving the first year and 60 per cent remaining alive 5 years after surgery. As anticipated, the survival outcome in other stages are poor, particularly in stage 3a giving a 1-yr and 5-yr survival of only 54 per cent, and 15 per cent, respectively. Our findings colloborate the notion that early surgical resection in early stage lung cancer is the only strategy in achieving a cure, if at all possible.

In line with our previous study on histologic types of lung cancer among Thai patients[2], adenocarcinoma is the most common cell type in the present report. It has been shown that adenocarcinoma of the lung is increasing and, in some reports, exceeds other histologic types[13-16]. In a multicenter series on 5,230 patients with non-small-cell lung cancer, adenoCA accounted for 53 per cent, whereas, squamous cell CA and large cell CA accounted for 41.6 and 3.6 per cent respectively[15]. Several factors may be implicated, the issue of which has been covered elsewhere[2,17]. The association between tobacco smoking and various histopathologic types has also been assessed in our previous study[2]. It is however beyond the scope of the present report to elaborate further.

By and large, the survival outcome among patients with NSCLC following resection in our study is comparable to other reports[4-7,15]. For example, the 5-yr survival in stage 1, 2, and 3a were 59 per cent, 30 per cent, and 16 per cent respectively in a recent report by Al-Kattan, et al[5]. These figures were essentially similar to ours. It should be noted, however, that squamous cell carcinoma predominated in the series of Al-Kattan et al (60%), followed by adenocarcinoma (30%)[5]. This survival similarity substantiates the notion that the survival curves of bronchogenic squamous cell carcinoma and adenocarcinoma did not significantly differ[4].

The similar survival outcomes in NSCLC following surgery among various series carry an extremely important message. In spite of the different health care facilities and the different referral systems, the survival outcome of lung cancer patients higher than stage 1 is uniformly poor. Therefore, the global efforts to diagnose and treat early stage disease remain the most important strategy to achieve cure, with any hope.

It is noteworthy that the difference in cumulative survival at 2 years and 5 years in stage 3a are only marginal, i.e 23 per cent and 15 per cent. This indicates that most patients with stage 3a survive less than two years. Conversely, those who survive two years are likely also to be alive at five years. The sharp drop in survival chance within the first two years in stage 3a reflects its aggressive nature both in terms of distant metastases and local invasiveness.

Criticisms could be made on the use of postal reply in our study. In an atmosphere of health care system like our country, centres with full facilities are not evenly situated across the nation. Patients receiving health services in our hospital are typically referred from all parts of the country; a proportion of the patients understandbly sought to receive post-operative follow-up at local health facilities. This renders long-term follow-up in all cases in any single referral centre virtually impossible. We therefore opted to employ a postal survey where necessary. The high return of response in our study, 70 per cent, is encouraging and proves that such an exercise is feasible and indeed useful.

It may be argued that the method of postal reply may have induced a selection bias towards more responses from those who were alive. As stated, the questionnaires were addressed to the patients and their next-of-kins. This selection bias has proved not to be the case in our study. The similar proportions of alive/ death status between the two sources, namely the medical records (22/29) and the postal reply (16/21), categorically refutes this theoretical argument.

Considering that the survival outcome following surgical resection in stage 2 and 3a is poor, the following measures should be taken to improve the survival benefit :

Firstly, prevention steps must be exercised and include a continued campaign against cigarette smoking, measures to protect passive smokers. Research into other aetiological factors should be encouraged in order that prevention of risk factors and modification of lifestyles be undertaken.

Secondly, diagnostic intervention in patients presenting with a lung mass should be expedited and, when necessary, referral should be made as early as possible. This is to ensure a diagnosis at an early stage, prompt surgical treatment, resulting in a better survival advantage.

Thirdly, research on therapeutic adjunct to improve survival benefit in stage 2 and 3a should be encouraged. These include the use of induction (formerly called neoadjuvant) chemotherapy[18-20]. The rationale for using induction chemotherapy is that the drugs can reach the tumour more easily, and will be more effective. Subsequent radiotherapy will be more effective against a smaller tumour, surgery is likely to be more succesful and less radical. Induction chemotherapy may also eradicate early micrometastases. In a recent trial employing preoperative chemoradiation in order to downstage and increase resection rate for stage 3a disease, 2-yr and 5-yr survivals were 66 per cent and 37 per cent, respectively[21]. These survival durations are undoubtedly longer than those achieved by surgical resection alone. Results from larger trials are awaited.

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การรอดชีพหลังการผ่าตัดปอด ในผู้ป่วยไทยด้วยโรคมะเร็งปอด

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ได้ศึกษาการรอดชีพหลังการผ่าตัดปอดในผู้ป่วยด้วยโรคมะเร็งปอดที่มารับการรักษา ณ โรงพยาบาลโรคทรวงอก ระหว่าง พ.ศ. 2531-2535. มีผู้ป่วยด้วยโรคมะเร็งปอดทั้งสิ้น 127 รายได้รับการผ่าตัดปอดในระยะเวลาดังกล่าว. อายุเฉลี่ย 60 ปี, เป็นชาย 103 ราย, หญิง 24 ราย. ชนิดเซลล์เป็น adenocarcinoma ร้อยละ 59, squamous cell carcinoma ร้อยละ 35, และ large cell carcinoma ร้อยละ 6. มีข้อมูลการรอดชีพในผู้ป่วยทั้งสิ้น 88 ราย, ยังมีชีวิตอยู่ 38 ราย, เสียชีวิตแล้ว 50 ราย. เป็นผู้ป่วย stage 1 จำนวน 47 ราย, stage 2 จำนวน 12 ราย, และ stage 3a จำนวน 29 ราย. การรอดชีพหลังการผ่าตัด 1 ปี, 2 ปี, และ 5 ปี เท่ากับ 85%, 78%, และ 60% ใน stage 1; 70 %, 50 %, และ 30% ใน stage 2; 54%, 23%, และ 15% ใน stage 3a [log rank 19.06, df 2, p = 0.0001].

คำสำคัญ : มะเร็งปอด, ศัลยกรรม, การรอดชีพ

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