

Survival of primary lung cancer patients in Brunei Darussalam, 1987–2012

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Background: In 2009 to 2011, the commonest cause of death was by cancer in Brunei Darussalam, and 16.5% and 19.5% of cancer deaths were due to lung cancer in 2004 and 2011 respectively. This study was to investigate the survival of lung cancer patients in Brunei Darussalam.

Methods: This retrospective cohort study was conducted in 2013 & 2014 for those who were diagnosed as primary lung cancer in the period of 1987 to 2012. Data were retrieved from patients' medical records and death certificates using pretested data collection form. Survival analyses namely Kaplan-Meier method, and log-rank test to compare survival between groups.

Results: We retrieved 630 primary lung cancer records. Majority was diagnosed at the late stages, 42.5% at Stage IV & 33.4% at Stage III. The overall median survival time was 6.1 months whereas 2.6 and 79.1 months for Stage IV and Stage I respectively. The overall 6-month, 1-, 3- and 5-year survival rates were 50.2%, 32.1%, 14.5% and 8.8% respectively. Survival duration had significantly improved from 1987–1999 to 2000–2012 ($P=0.001$) although significant higher proportion of Stage IV was diagnosed in the second period ($P=0.008$).

Conclusions: Overall survival rates and duration of primary lung cancer in Brunei Darussalam were comparable with some developed countries. However, through effective public intervention such as increase awareness, early case detection, and effective anti-smoking strategies, survival of lung cancer patients can certainly be improved and the burden of disease can be reduced.

Keywords: Primary lung cancer; survival rates; survival duration; Brunei Darussalam

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Introduction

GLOBOCAN 2008 reported that, there were 1.6 million new cases of lung cancer (12.7% of total cancer cases) and nearly 1.38 million deaths (18.2% of total cancer deaths) worldwide (1). Four years later, GLOBOCAN 2012 reported that 1.8 million new cases of lung cancer were estimated in 2012, which accounted for 12.9% of the total cancer cases worldwide. It was also estimated 1.59 million deaths from lung cancer contributing to 19.4% of total cancer deaths in

the same year. Lung cancer had been not only the most common cancer but also the most common cause of death from cancer worldwide. The overall ratio of mortality to incidence was 0.87, and considered a highly fatal cancer (2).

Didkowska *et al.* reported that lung cancer death worldwide was expected to increase to 2.9 million in 2035 (increase by 86% comparing to 2012). Though the scale of increase was different, the increase was expected in all regions. The increase was predicted to be highest in East Mediterranean region (by 123%) and Africa region (by 108%) (3).

Similarly in Brunei Darussalam, from 2004 to 2011, primary lung cancer was the most common cause of death among all cancers. It led to 16.5% and 19.5% of all cancer deaths in 2004 and 2011 respectively (4-6). Furthermore, the lung cancer mortality had increased from 9.1 per 100,000 population in 2009 to 12.7 in 2011 (6).

With this increasing burden of lung cancer worldwide, similarly in Brunei Darussalam, it is important to study survival of lung cancer patients as it reflected the effectiveness of the management of lung cancer (7). Though incidence and mortality was on the rise worldwide, survival of lung cancer patients had increased in several countries such as United States, United Kingdom (UK), Denmark, Australia, Canada and Singapore (8-11). One of the major factors which have great impact on the survival is the stage of cancer at the time of diagnosis (12). Unfortunately, most lung cancer patients were diagnosed at the advanced stage. For instance, more than 70% of patients were diagnosed in Stage III and Stage IV in the United States and Singapore (13,14).

To our knowledge, there was little information available on survival of lung cancer patients in Brunei Darussalam. Therefore, we aimed to investigate the survival of primary lung cancer patients from 1987 to 2012 in Brunei Darussalam, specifically, to determine survival rates and median survival times, the stages of cancer at the time of diagnosis, and differences of stages and survival between the first and second half of the study period to determine the trend.

Methods

Study design

This retrospective cohort study was conducted in 2013 & 2014, using 26-year recorded data from 1987 to 2012 in Brunei Darussalam.

Study population

We aimed for all primary lung cancer patients diagnosed in Brunei Darussalam as the reference population. As all cancer cases were recorded in the four district hospitals, and the Brunei Cancer Centre in Brunei Darussalam, all recorded cases were retrieved from the five institutions. Primary lung cancer cases diagnosed during the period from the beginning of 1987 to the end of 2012 were included without any exclusion criteria or sampling.

Data collection

A pretested data collection form was used to collect the data from medical record. Death information such as date and cause of death, were obtained from patients' death record in the medical records and verified by death certificate obtained from the Immigration and National Registration Office of Brunei Darussalam.

Data collection form

We designed the data collection form, first by reviewing National Lung Cancer Clinical Audit form (15) and adding some additional information required for this study. Then, the form was pretested by collecting 20 cases without experiencing any significant difficulties. The form basically included demographic information of patients, smoking history, staging of cancer using the 6th TNM lung cancer staging (16), histology type and date of death or last seen.

Data analysis

Data entry and analyses were done using IBM SPSS version 20.0.0. (17). Descriptive statistics were used appropriately to describe numerical and categorical information of the study population. With regard to survival analyses, patients who died with primary lung cancer or complications of primary lung cancer were considered as events whereas those who were still alive at the last-seen date or died with caused of death other than primary lung cancer (e.g., car accident, heart attack) were considered as censored. The Kaplan-Meier method was used to analyse survival rates, survival duration and survival curve. Comparison of survival was done using log-rank tests.

Ethical considerations

This study was approved by the Medical and Health Research and Ethics Committee (MHREC) of Ministry of Health, Brunei Darussalam [Ref: MHREC/EDU/2011/10 (3), dated 16-Jun-2011]. The chief executive officer (CEO) of each hospital also gave permission to conduct the study. The Immigrations and National Registration office of Brunei Darussalam also gave permission to access patients' date of and cause of death on their database.

Table 1 Demographic characteristics and smoking status of study population

Variable	n (%)
Age	
≤30	2 (0.3)
31–40	15 (2.4)
41–50	72 (11.4)
51–60	134 (21.3)
61–70	180 (28.6)
71–80	163 (25.9)
81–90	60 (9.5)
≥91	4 (0.6)
Gender	
Male	380 (60.4)
Female	250 (39.6)
Nationality	
Bruneian nationality	521 (82.8)
Permanent resident	85 (13.4)
Foreigners	24 (3.8)
District	
Brunei-Muara	344 (64.3)
Tutong	91 (17.0)
Kuala Belait	78 (14.6)
Temburong	22 (4.1)
Race	
Malay	441 (70.3)
Chinese	96 (15.3)
Indigenous	74 (12.2)
Others	14 (2.2)
Tobacco use	
Known smoker	402 (76.9)
Never smoker	121 (23.1)

Results

Demographic characteristics and smoking history

There were 630 primary lung cancer cases diagnosed during the period (1987 to 2012) and all were included.

There were 137 cases diagnosed during the first 13 years (1989 to 1999) and 493 cases during the second 13 years (2000 to 2012).

Table 1 shows the distribution of demographic characteristics and smoking history. The mean age was 65 (SD 12.4) years old, ranging from 26 to 92 years. Majority was age between 51 and 80 (75.8%), male (60.4%), Bruneian (82.8%), residing in Brunei-Muara district (64.3%), Malay ethnic group (70.3%) and smokers (76.9%).

Stages of lung cancer & histology at time of diagnosis

The distribution of stages at diagnosis for 598 primary lung cancer cases is presented in *Table 2*. A total of 32 cases (5.1%) could not be included in the analysis as their stages were not stated in the records. From 1987 to 2012, majority of cases was diagnosed at Stage IV (42.5%), followed by Stage III (33.4%), Stage II (5.3%), and Stage I (9.2%). A significant higher proportion was diagnosed at late stage of cancer (Stage IV) in the second period (2000–2012) as compared to the first period (1987–1999) (43.4% versus 38.8% respectively, $P=0.008$).

The distributions of type of histology are presented in *Table 2*. A significant higher proportion of non-small cell lung cancer was diagnosed in the second period as compared to the first period (90.9% versus 83.5% respectively, $P=0.012$).

Survival of lung cancer patients

There were nine cases (1.4%) missing medical records after diagnosis and therefore, their survival durations could not be included in the analysis. The overall survival curve for 621 lung cancer patients (*Figure 1*) shows the rapid loss of survival after a few months of diagnosis. The median survival time was 6.1 months.

The survival rates and median survival time in month, and the comparison of these survival data between the two periods are presented in *Table 3*. Survival rates and median survival time of patients diagnosed in the second period had improved significantly ($P=0.001$) compared to the first period.

Specific median survival times for each stage of primary lung cancer for the whole study period, and also for each of two periods are reported in *Table 4*. In both overall and two periods, significant reduction of survival was observed as the cancer stage became more advanced. Specific survival curves for various stages for the study period are presented in *Figure 2*.

Table 2 Stages and histology of primary lung cancer diagnosed in the study period

Stage & histology	1987–2012, n (%)	1987–1999, n (%)	2000–2012, n (%)	Comparison of two periods [†]
Stages at diagnosis				$X^2 = 20.7$; $df = 8$; $P = 0.008^{\ddagger}$
Stage IA	27 (4.5)	0 (0.0)	27 (5.6)	
Stage IB	28 (4.7)	2 (1.7)	26 (5.4)	
Stage IIA	6 (1.0)	1 (0.9)	5 (1.0)	
Stage IIB	26 (4.3)	6 (5.2)	20 (4.1)	
Stage IIIA	33 (5.5)	4 (3.4)	29 (6.0)	
Stage IIIB	167 (27.9)	39 (33.6)	128 (26.6)	
Stage IV	254 (42.5)	45 (38.8)	209 (43.4)	
Limited	17 (2.8)	7 (6.0)	10 (2.1)	
Extensive	40 (6.7)	12 (10.3)	28 (5.8)	
Total	598 (100.0)	116 (100.0)	482 (100.0)	
Lung cancer histology				$P = 0.012^{\S}$
NSCLC	538 (89.4)	101 (83.5)	437 (90.9)	
SCLC	57 (9.5)	19 (15.7)	38 (7.9)	
Mesothelioma and other carcinoids	7 (1.1)	1 (0.8)	6 (1.2)	
Total	602 (100.0)	121 (100.0)	481 (100.0)	

[†], “two periods” refers to 1987–1999 vs. 2000–2012; [‡], Chi-square test; [§], Fisher’s exact test. NSCLC, non-small cell lung cancer; SCLC, small cell lung cancer.

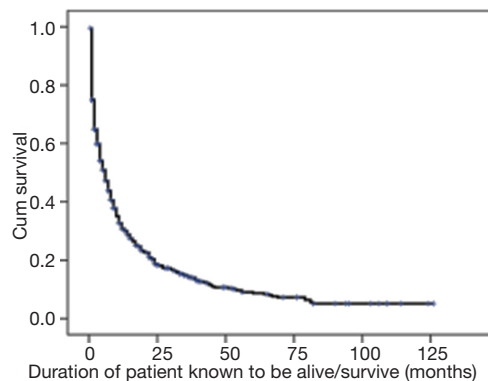


Figure 1 Survival curve (Kaplan-Meier) of primary lung cancer during the study period (1987 to 2012) (n=621)

Discussion

There were only 137 cases (21.7%) diagnosed during the first 13 years but 493 cases (78.3%) in the second 13 years.

Though there was no clear evidence for too low number of cases in the first period, we believe that this could be due to not seeking medical treatment in those days. This could be the same reason for the lower proportion of Stage IV during the first period than the second period. It might not be due to lack of diagnostic facilities as the medical facilities had been already equipped with CT scanners since 1986. Another reason could be poor hospital record system and missing records in those days especially after death of patients. What we obviously knew was that the hospital record system was improved and cancer registry was also established during the second period. Nevertheless, as we found in the literature worldwide (1-3), we believe that the incidence had increased to a certain extent throughout the study period.

Table 5 tabulates the comparison of distribution of stages between current and previous studies. Distribution of stages of both periods of current study was similar to other studies done in Singapore (14), US (9,13), UK (12), and Spain (18).

Table 3 Survival rates and duration of primary lung cancer diagnosed in the study period

Year of diagnosis	1987–2012 (n=621)	1987–1999 (n=137)	2000–2012 (n=484)	Comparison of two periods [†]
Survival rates [‡] (%)				$\chi^2 = 10.99$; $df = 1$; $P = 0.001$
6-month	50.2	42.7	52.3	
1-year	32.1	24.5	34.1	
3-year	14.5	7.0	16.4	
5-year	8.8	4.0	10.1	
Median survival time in months	6.1	4.4	6.7	
(95% CI)	(5.0, 7.1)	(2.8, 5.9)	(5.5, 7.8)	
No. of events	516	119	397	
No. of censored	105 (16.9%)	18 (13.1%)	87 (18.0%)	

[†], comparison of survival between two periods (1987–1999 vs. 2000–2012) using log-rank test; [‡], using Kaplan-Meier method.

Table 4 Median survival time by stages of cancer for the study periods

Stage of cancer	Median survival time (in months)		
	1987–2012 (n=591)	1987–1999 (n=117)	2000–2012 (n=474)
Stage I	79.1	79.1	81.0
Stage II	19.4	14.4	23.5
Stage III	8.3	8.8	8.3
Stage IV	2.6	2.1	2.8
SCLC	3.4	2.8	4.4
Comparison by stages [†] using log-rank test	$\chi^2 = 167.3$, $df = 4$, $P < 0.001$	$\chi^2 = 32.80$, $df = 4$, $P < 0.001$	$\chi^2 = 136.2$, $df = 4$, $P < 0.001$

[†], comparison among five categories above. SCLC, small cell lung cancer.

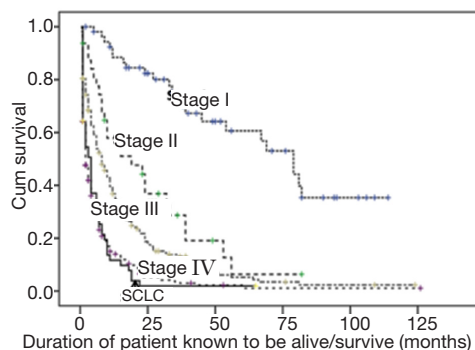


Figure 2 Survival curve (Kaplan-Meier) by stages of primary lung cancer during the study period (1987 to 2012) (n=621). SCLC, small cell lung cancer.

This implies that early detection of lung cancer has been a big challenge even in the developed countries. This indicates that primary prevention of lung cancer is greatly important to reduce the burden of lung cancer. New method of early detection which is affordable, less invasive, easy to conduct (e.g., salivary biomarker) will be highly valuable.

Table 6 presents comparison of survival between countries from previous studies. For the period of 1987–1999, the 5-year survival of our study was poorer than other studies done in US (9), Denmark (20), UK (10) and Australia (10). However, for the period of 2000–2012, our result was comparable with Denmark (10) and UK (10) but poorer than Australia (10) and US (9). Similar pattern could be

Table 5 Comparison of TMN stages at diagnosis between current and previous studies

Country	Year of diagnosis	Percentage				
		Stage I	Stage II	Stage III	Stage IV	Others
Brunei Darussalam	1987–1999	1.7	6.1	37.0	38.8	16.3 [†]
Singapore women (14)	1996–1998	8.3	4.9	32.5	38.0	16.3 [‡]
US (13)	1998–2003	15–18	2–3	30–39	44–52	–
US (9)	2002–2008	–	–	–	56.0	–
UK (12)	2004–2007	14.8	7.3	29.5	48.4	–
Spain (18)	2003	14.6–17.7	2.9–4.0	35.3–40.3	37.3–46.9	1.1–2.9 [‡]
Brunei Darussalam	2000–2012	11.0	5.1	32.6	43.4	7.9 [†]

[†], small cell lung cancer; [‡], unknown. US, United States; UK, United Kingdom.

Table 6 Comparison of survival rates between current and previous studies

Country	Gender	Year of diagnosis	Survival rates (%)			
			6-month	1-year	3-year	5-year
Brunei Darussalam	Both	1987–1999	42.7	24.5	7.0	4.0
US (9)	Both	1984–1986	–	–	–	13.1
US (9)	Both	1993–1995	–	–	–	14.4
Singapore (14)	Women	1996–1998	–	36.0	16.0	–
Denmark (19)	Men	1994–2003	–	30.0	–	8.0
Denmark (19)	Women	1994–2003	–	34.0	–	9.0
UK (10)	Both	1995–1999	–	23–27	–	6.9–9.7
Australia (10)	Both	1995–1999	–	37.8–38.6	–	13.4–14.2
Brunei Darussalam	Both	2000–2012	52.3	34.1	16.4	10.1
Spain (18)	Both	2003	–	36.2	13.8	–
Denmark (10)	Both	2005–2007	–	35.0	–	0.11
UK (10)	Both	2000–2002	–	25.9–27.5	–	7.6–8.1
UK (10)	Both	2005–2007	–	28.5–30.6	–	8.7–11.0
Australia (10)	Both	2000–2002	–	39.9–41.5	–	13.6–16.2
Australia (10)	Both	2005–2007	–	42.7–42.9	–	16.2–17.6
US (9)	Both	2002–2008	–	–	–	16.9

US, United States; UK, United Kingdom.

seen for 1 year-survival rate.

In this study, majority of primary lung cancer cases was diagnosed at between 51 and 80 years old, the youngest age was 26, two (0.3%) were below 30, and 17 (2.7%) were

below 40. Though the mean age (65 years) at diagnosis in Brunei was comparable with the report for Singaporean women (65.3 years) (14), it was younger than the studies done in European countries, Australia and Canada where

the mean age was 70.3 years (10). It is worth to investigate whether Bruneians were more susceptible for lung cancer at younger age.

The major weakness of the current study was possible missing cases especially in the first period (1987–1999) of study. However, the second period (2000–2012) data gave much reliable and valid information. It also had minimal and acceptable number of censored cases as lung cancer cases did not have long survival.

In overall, the survival of the current study was acceptable as it was comparable with some of the developed countries. However, survival still can be improved through early detection by adopting effective public health strategies such as by increasing public awareness of lung cancer, and guidelines for regular medical check-up for various risk groups. Finally effective anti-smoking campaign through public education will help to reduce overall burden of the disease.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

Ethical Statement: This study was approved by the Medical and Health Research and Ethics Committee (MHREC) of Ministry of Health, Brunei Darussalam [Ref: MHREC/EDU/2011/10 (3), dated 16-Jun-2011]. The chief executive officer (CEO) of each hospital also gave permission to conduct the study. The Immigrations and National Registration office of Brunei Darussalam also gave permission to access patients' date of and cause of death on their database.

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