RESEARCH COMMUNICATION

Respiratory Cancer Population-Based Survival in Mumbai, India

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Abstract

Survival experience of patients with cancer of the larynx (ICD-32) or lung (ICD-34) registered by the Mumbai (Bombay) population based cancer registry, India, during the years 1992-94 was determined. The vital statistics of the patients were established by matching with death certificates from the Mumbai Municipal death register and by active methods such as telephone enquiry, reply-paid postal enquiry, house visits and scrutiny of case records. Of the 1905 (675 larynx and 1230 lung) eligible cases for analysis, 1480 were dead (450 larynx and 1030 lung) and 425 were alive (225 larynx and 200 lung). The overall 5-year observed and relative survival rates for laryngeal cancers were 29.1% and 36.4%, and for lung cancers were 12.5% and 15.9% respectively. On multivariate analysis, age, treatment and clinical extent of disease emerged as independent predictors of survival with both cancers. People aged 55 years and above had a relative risk of four or more for laryngeal cancer and 2.3 times and more for lung cancer death as compared to those aged less than 35 years. Early detection and prompt treatment should improve overall survival from lung as well as laryngeal cancer.

Key Words: Survival - laryngeal cancer - lung cancer - control - age - treatment

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Introduction

In countries where population based cancer registries have been established for several decades, survival of cancer patients has been increased dramatically for many cancer sites. (Dickman et al 1999, Millar et al 1992). Cancer however is still a highly lethal disease. In present paper an attempt has been made to estimate the survival at five years from diagnosis for two main respiratory cancers, of the lung and larynx, registered in Greater Mumbai during 1992 to 1994.

Lung cancer is the most common tumour worldwide with 900,000 new cases in each year in men and 330,000 in women. It is also the leading cause of death from cancer. (Ferlay et al 2001). In Greater Mumbai also in males lung as single organ was found most vulnerable to cancer (Kavarana et al, 2003). Larynx occupies 15th rank worldwide with 403,000 new cases in men and 54,000 in women showing more burden in developing world than developed world (Ferlay etal). In Mumbai it ranks 6th in incidence amongst men (Kavarana et al, 2003).

A total of 1428 subjects with cancer of lung (1112 males, 316 females) and 823 with cancers of larynx (698 males, 125 females) were registered in Greater Mumbai during 1992-94. These two neoplasms contribute 89.7 % of respiratory cancers (lung 56.9% and larynx 32.8%). Lung cancer has the poorer prognosis and smoking is an etiological factor for both. Occupational exposure and air pollution make minors contribution to their incidences. Results obtained in the present study were compared with those in other populations. Particularly for laryngeal cancers, survival rates appear always better for populations in developed countries when compared with the rates for developing countries.

Materials and Methods

The Mumbai Cancer Registry the first population based country to be established in India in 1963, registers all new cancer cases occurring in the residential population of Mumbai (currently 11 million) in Western India. The registry staff visit more than 150 data sources comprising hospitals/ clinics/laboratories. Data on sex, address, religion, education, marital status, age at diagnosis, incidence, site, histology, clinical extent of disease and treatment are abstracted from the hospital/clinic-medical records.

Data from death certificates mentioning "Cancer" or "Tumour" obtained from the Bombay Municipal Corporation Vital Statistics Office are also abstracted and processed. When the registry on the bases of death certificates first identifies cancer cases, these cases are matched with existing patient incidence files in the registry. If no match is found

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then efforts are undertaken to trace back these cases to hospital and clinic records. If death certificates notifications cannot be traced back to hospital records, it is assumed that theses patients probably never received any significant medical care when they were alive. Such cases are registered on the basis of information available in the death certificates only (DCO) The data collected are entered in the computer and processed for elimination of duplicate registrations, validity checks and analysis. Quality control exercises are regularly undertaken to ensure the validity, reliability and completeness of the data (Yeole 2001).

A total of 823 subjects with laryngeal and 1428 subjects with lung cancer were diagnosed for the period of 1992 to 1994. Of these, 513 (62.3% for larynx) and 872 (61.1% for lung) cancers were diagnosed on the basis of confirmation by histology. 162 (20.6% for larynx) and 358 (25.1% for lung cancer) were diagnosed by clinical examination only. 148 (18% of larynx) and 198 (13.8 for lung cancer) were diagnosed on the basis of information available in DCO. After the exclusion of DCO cases where date of incidence and date of death are assumed to be same day (thus 0 survival) 675 cases for larynx and 1230 cases for lung were eligible for the further analysis.

A variety of active and passive follow up methods were used to establish the vital status of patient. The cases were matched against death certificates mentioning "cancer" for the period 1992-1999 from Bombay Municipal Death Registration Office to identify those who might already have died. Of cases for which no matching death certificated found, reply-postal or telephone enquires were made regarding the current status of their health. For those cases no information on their vital status after these efforts home visit were carried out by social workers employed by the registry. For patients who could not be stressed out by house visits, case records from reporting hospitals were scrutinized to detereming the date of their last clinic visit and their status during that visit.

The survival of each case was determined by the time difference between the date of incidence and date of death or of last follow up. Cumulative observed and relative survival probabilities were calculated using Hakulinen's method (Hakulinen 1982, Hakulinen et al 1994) To calculate observed survival death from any cause of taken as failure and the subjects were known to be alive on their last follow-up were censor on theses deaths. Relative survival which indicates the proportion of people who risk dieing from the disease, in question, was calculated as the ration of observed to expected survival in a group of people in the general population similar to the diseased group with respect of age, sex, and calendar period of observation. The expected survival was calculated based on live table constructed from the mortality from all causes of death in Mumbai (Annual Report-BMC 1990)

To compare the results of the study with those in other populations, age-standardized relative survivals (ASRS) was calculated by directly standardizing relative survival to the specific age distributions of the estimated global incidence of major cancers of 1985 (Black & Bashir 1998). The log rank test was used in a univariate analysis to identify potentially important prognostic variables. The variables that showed statistical significance on univariate analysis were introduced stepwise into Cox regression model to identify the independent predictors of survival. (Cox 1972).

Results

Of the 1905 (675 larynx and 1230 lung) eligible cases for analysis 1480 were dead (450 larynx and 1030 lung) and 425 were alive (225 larynx and 200 lung). On the last date of follow-up of the later 130 patients (65 laryngeal and 75 lung) were last to follow-up during the five years after the index date. Thus complete follow-up details for 5 years after incidence date was available for 92.7% (n=1765, larynx 610 and lung 1155) of included cases.

The overall five year observed and relative survival rates for laryngeal cancer were 29.1% and 36.4% and for lung cancer 12.5% and 15.9% respectively. (Table 1). Five-year relative survival data by age for both cancers are given in Table 2. With advance in age relative survival decreased for both cancers. There were no survival differences between males and females. There was a rapid decline in survival in the first two years, after diagnosis. Data for 5-year observed survival by sex, age, religion, marital status, education, clinical extent of disease and treatment are given in Table 3. Information on clinical staging was available for 90% (94% larynx and 89% for lung) of cases. Treatment details were not available for 1/3 of the cancers. In the larynx a third of cancers were classified as localized and half of them were

Table 1. Observed and Relative Survival for Larynx and Lung Cancer Cases, Greater Mamba, 1992-1994

Site	Number	Observed Survival (%)			Relative Survival (%)		
		1 Year	3 Year	5 Year	1Year	3 Year	5 Year
Larynx	675	59.6	36.7	29.1	62.3	42.0	36.4
Lung	1230	29.9	15.9	12.5	31.3	18.3	15.9

Table 2. Five-Year Relative Survival for Larynx and Lung Cancer Cases by Age, Greater Mumbai 1992-1994

Site	5-Year Relative Survival (%)						5 Year ASR (%)	
	<35	35-44	45-54	55-64	65-74	75+	All Ages	0-74
Larynx	72.9	40.5	39.2	35.1	30.7	20.6	33.0	37.0
Lung	43.8	16.8	23.2	13.4	7.8	0.0	9.9	14.6

Table 3. Five Year Observed Survival Rates for Cancers of Larynx and Lung, Greater Mumbai, 1992-1994.

Variable	Larynx			Lung		
	Number	Survival (%)	P value	Number	Survival (%)	P value
Sex			0.629			0.489
Male	574	29.4		983	12.3	
Female	101	25.8		247	13.4	
Age			<0.0001			<0.0001
<35	19	71.4		42	42.9	
35-44	65	39.2		94	16.3	
45-54	152	36.3		249	21.8	
55-64	206	29.8		397	11.0	
65-74	166	21.3		321	5.3	
75+	67	8.4		127	0.0	
Marital Status			0.0314			0.0060
Single	24	35.5		50	17.7	
Married	553	28.9		1021	13.4	
Widowed	64	16.9		100	2.4	
Others/Unk.	34	46.7		59	7.1	
Religion			0.0823			0.0005
Hindu	465	29.8		842	12.3	
Muslim	131	33.3		227	17.5	
Christian	48	17.1		103	5.8	
Others	2	0.0		4	0.0	
Education			0.0089			0.0001
None	111	23.5		129	13.1	
<6 years	106	18.2		136	18.8	
6-12 years	123	30.8		214	14.1	
>12 years	21	42.2		44	9.3	
Unknown	314	33.1		707	10.9	
Extent of Dis			<0.0001			<0.0001
Localized	226	53.1		481	28.0	
Regional	378	17.8		242	3.1	
Distant Met.	30	0.0		366	0.6	
Treatment			<0.0001			<0.0001
Surgery	74	40.4		67	22.6	
Radiotherapy	218	33.6		227	7.5	
Chemo	16	31.1		108	17.4	
Combined	79	29.6		91	11.4	
Others	47	13.7		160	10.7	
Unknown	241	24.5		577	12.6	

classified as regional disease while in lung 30% of cases had distant metastasis.

Relative survival by different clinical stages is presented in Figure 1 for larynx and in Figure 2 for lung. For laryngeal cancer the five-year survival was less than 30% for those aged 55 years and above while it was 71.4% for those age under 35 years. The five year survival was 53.1% for localized cancer 17.8% for regionally spread cancers. For lung cancer the five years survival was only 11% for those age 55 years and above while it was 43% for those age under

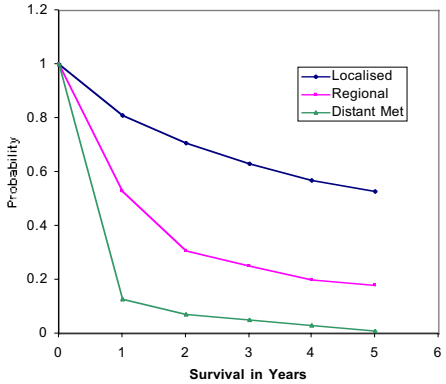

Figure 1. Survival from Laryngeal Cancer

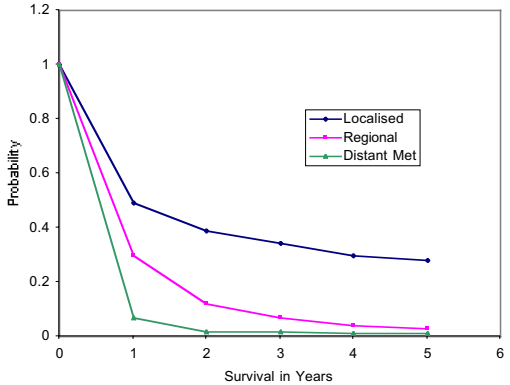

Figure 2. Survival from Lung Cancer

Table 4. Independent Predictors of Survival From Larynx Cancer in Mumbai 1992-1994

Factor	Univariate		Multivariate	
	Hazard Ratio	Conf. Interval	Hazard Ratio	Conf. Interval
Age Group				
<35	1.00		1.00	
35-44	3.00	1.18-7.62*	2.64	1.02-6.87*
45-54	3.14	1.28-7.73*	2.69	1.06-6.84*
55-64	4.03	1.65-9.84*	4.08	1.62-10.27*
65-74	4.71	1.92-11.52*	4.14	1.64-10.48*
75+	6.54	2.02-16.33*	5.32	2.07-13.71*
Marital Status				
Single	1.00		1.00	
Married	1.14	0.68-1.99	0.85	0.50-1.47
Widowed	1.49	0.84-2.66	0.94	0.50-1.75
Unknown	0.67	0.33-1.35	0.54	0.26-1.11
Education				
Illiterate	1.00		1.00	
<6 years	1.13	0.82-1.53	1.43	1.03-1.97*
6-12 years	0.72	0.53-0.99*	0.92	0.67-1.28
>12 years	0.50	0.26-0.93*	0.76	0.40-1.47
Unknown	0.84	0.64-1.09	1.18	0.89-1.57
Extent of Dis.				
Localized	1.00		1.00	
Regional	2.81	2.23-3.53*	3.48	2.73-4.45*
Distant Mets	8.03	5.13-12.15*	6.19	4.05-9.46*
Unknown	4.13	2.76-6.19*	4.12	2.71-6.27*
Treatment				
Surgery	1.00		1.00	
Radiotherapy	1.10	0.78-1.54	0.96	0.68-1.36
Chemo	1.51	0.76-3.00	1.37	0.68-2.76
Combined	1.18	0.79-1.77	1.05	0.70-1.59
Others	2.18	1.42-3.34*	2.07	1.32-3.20*
Unknown	1.74	1.25-2.41*	1.86	1.32-2.61*

35 years. The five years survival was 28% for localized cancer and 3% for regionally spread cancers.

On univariate analysis survival differences reached statistical significant for age, education, treatment, extent of disease for larynx and age, religion, treatment and extent of disease for lung cancers (Tables 4 & 5). On multivariate analysis age, treatment and clinical extent of disease immerged as independent predictors of survival for both the cancers. People aged 55 years and above had the relative risk of four or more for laryngeal cancers and 2.3 times and more lung cancer for death as compared to those aged less than 35 years.

Discussion

Population-based survival data are useful to assess the efficiency of cancer related health services available in a given region. It indicates the average outcome from a given cancer; all cases diagnosed in a given population are included in the analysis. Cases with different natural histories, stage distribution and treatment profiles, as well as follow-up care patterns are included in population based cancer survival analysis. It reflects the some total of the impact of health care in terms of early detection, access to diagnosis, treatment and follow-up care on outcome.

Table 5. Independent Predictors of Survival From Lung Cancer in Mumbai 1992-1994

Factor	Univariate		Multivariate	
	Hazard Ratio	Conf. Interval	Hazard Ratio	Conf. Interval
Age Group				
<35	1.00		1.00	
35-44	2.03	1.28-3.21*	1.75	1.09-2.80*
45-54	1.78	1.16-2.73*	1.72	1.11-2.67*
55-64	2.13	1.52-3.48*	2.12	1.38-3.25*
65-74	2.88	1.90-4.37*	2.66	1.72-4.10*
75+	3.99	2.57-6.19*	3.65	2.31-5.77*
Marital Status				
Single	1.00		1.00	
Married	0.93	0.68-1.28	0.94	0.67-1.32
Widowed	1.19	0.82-1.72	1.17	0.78-1.74
Unknown	1.39	0.93-2.04	1.20	0.78-1.86
Education				
Illiterate	1.00		1.00	
<6 years	0.96	0.73-1.26	1.05	0.79-1.37
6-12 years	1.01	0.80-1.28	1.01	0.79-1.30
>12 years	1.05	0.73-1.51	1.04	0.71-1.51
Unknown	1.37	1.12-1.67*	1.21	0.97-1.50
Religion				
Hindu	1.00		1.00	
Muslim	0.81	0.68-0.95*	0.82	0.69-0.97*
Christian	1.37	1.10-1.71*	1.24	0.99-1.55
Others	1.10	0.83-1.35	0.92	0.69-1.24
Extent of Dis.				
Localized	1.00		1.00	
Regional	1.86	1.57-2.21*	1.97	1.65-2.36*
Distant Mets	3.17	2.71-3.72*	3.21	2.73-3.78*
Unknown	2.05	1.65-2.54*	1.91	1.53-2.38*
Treatment				
Surgery	1.00		1.00	
Radiotherapy	1.62	1.18-2.22*	1.42	1.03-1.97*
Chemo	1.30	0.91-1.86	1.23	0.86-1.77
Combined	1.25	0.87-1.80	1.12	0.77-1.61
Others	1.90	1.36-2.64*	1.61	1.15-2.25*
Unknown	1.83	1.36-2.47*	1.69	1.24-2.29*

The larynx plays the important role in phonation, respiration and protection of the lower respiratory track. The larynx is composed of nine cartilages connected together by ligaments and moved by several muscles. It is lined by a mucous memberant, which continues with oropharynx above, and trachea below. The laryngeal subdivision of glottic supra- and sub-glottic regions form the basis of anatomical classifications of laryngeal cancers. The glottic laryngeal cancers are diagnosed at an early stage due to the

Table 6. Observed Survival by Sub Site for Laryngeal Cancer

Sub site	No. of Case	Observed survival % 1 Year	3 Year	5 Year	P value
Glottic	173	81.3	63.3	52.1	
Supraglottic	215	58.9	32.4	24.2	<0.001
Transglottic	287	46.5	24.5	19.4	
Larynx	675	59.2	36.7	29.1	

Table 7. 5-Year Age Standardized Relative Survival in 0-74 Year Age Group in Selected Populations

Population/Country	Period	Larynx	Lung
Mumbai, India	1992-94	37.0	14.6
Madras, India	1984-89	39.9	7.5
Chiangmai, Thailand	1983-99	25.8	3.1
Khonken, Thailand	1985-92	34.9	10.1
Europe	1985-89	62.2	9.9
USA, All races	1967-73	67.8	14.1
England	1985-89	66.0	7.1
Finland	1985-89	60.2	11.2
Sweden	1985-89	73.6	9.6

early manifestation of symptoms. Early symptoms such as hoarseness of voice or dysphonia or due to the changes in the vibrating characteristics of vocal cords as result of the growth. On the other hand, supra glottic and sub glottic cancers are more advances than glottis cancers at the time of diagnosis, because they usually do not produce early symptoms such as hoarseness. Supra and sub glottic cancers are associated with a high frequency of regional lymph node metastasis in view of the extensive lymphatic drainage.

Lung cancer survival depends upon clinical stage and pathology of tumor. Sputum cytology and radiology scans are the only non-invasive methods of detecting early cancers. Sensitivity can be variable dependent on histological type (greater for small cell and squamaus cell carcinoma) tumour site and location. (Lam & Shibuya 1999, Sankarnarayanan et al 1998). Sputum cytology may be appropriate for certain clearly define proofs or individuals at risk of lung cancers. Currently, however, there are no practicable and effective procedures available to provide population-based screening for lung cancers.

The signs and symptoms of lung cancer depend on the location of the tumour, the spread and effects of metastatic growth. Many patients are diagnosed on the basis of asymptomatic lesion discovered incidentally on X-ray. Symptoms indicative of the primary tumour include fatigue, decreased activity, persistent cough, labored breathing, chest pain, decreased appetite and weight lost.

Principal histological types of lung cancer are squamas cell carcinoma, adeno- carcinoma, large cell carcinoma and small cell carcinoma. The first three are also referred to as " non-small cell" lung carcinomas. Squamus cell carcinomas arises in proximal segmental branchi and is associated squamus metaplasia. Large cell carcinoma often appears in the distal branchi and it generally undifferentiated. Small cell carcinoma typically arises in the central endobronchial location and is commonly aggressive and invasive; frequently metastases are present at diagnosis.

Survival in laryngeal cancer is inversely related to tumour size and the extent of regional lymph node involvements. Glottic cancers are most curable in all head and neck cancers in view of possibility of early diagnosis and low frequency of lymphatic spread. In Bombay, glottic cancers were associated with a three-fold higher survival as compared to supraglottic and transglottic cancers (Table-6)

Age emmerged as a prognostic factor for laryngeal cancers as well as lung cancers in Mumbai. Those aged 55 years and above when constituted two-thirds of the laryngeal cancer patients in Mumbai, had very poor survival prospects. The overall survival of a laryngeal cancer patients (36.4%, 5-year relative survival) in Mumbai is due to the high proportion of patients with supra and transglottic (75%), regional disease (60%) and patients who are advanced in age 55 years and above.

For lung cancer those aged 55 years and above constituted about 70% of the lung cancer patient population in Mumbai had a very poor survival rates as compare to patients having age less than 55.

A comparison of 5-year Age Specific Relative Survival Ratios among selected population in India, Thailand and United States (US) for laryngeal and lung cancers is shown in Table 7 (Shanta et al 1998, Martin et al 1998, Vatanasapt 1998, Berrino et al 1995, Miller et al 1993, Sanakarnarayanan et al 2003, Yeole & Ramanakumar 2004). A higher 5-year survival rates was observed in Europe and US, while it was much lower in India and Thailand for both the cancers. The regional differences in the distribution of prognostic factors, particularly the clinical spread of disease, early detection efforts, and access to diagnosis and treatment may contribute to the observed variation s in cancer survival across these different populations. The poor survival in Mumbai and other developing populations are mostly related to high proportion of locally advanced disease.

Detecting laryngeal and lung cancer in early stages, when amenable to single modality therapies, offers the best chance of improving survival from this cancers. Major gains in survival could be achieve in Mumbai and other developing countries by sustained efforts in early detection and providing adequate loco-regional treatment. Measures to prevent second primary cancers and primary prevention by tobacco/alcohol control measures should receive attention in the overall control of lung and laryngeal cancers.

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