RESEARCH ARTICLE

Low Lung Cancer Resection Rates in a Tertiary Level Thoracic Center in Nepal - Where Lies Our Problem?

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Abstract

Background: Resection rates of lung cancer are low in general and especially in countries like Nepal. Advanced stage at presentation and poor general condition of the patient are the usual causes. Materials and Methods: In this prospective observational study, one hundred cases of lung cancer who presented at the Thoracic Surgery Unit between October 2011 and October 2012 were included. Results: Those aged in the 6th and 7th decades together accounted for 72/100 patients. The male to female ratio was 2:1. There was a mean-29.2±14.2 pack yrs smoking history with only five non-smokers. Seventy-six patients presented with locally advanced disease while 21 had metastases. Only three had local disease. The average time between onset of symptoms to first contact with a doctor was 2.3±5.3 months (range: 0-35.6 months). Average time between first contact to referral was 50.4±65.7 days (range-0-365). Only three patients were resected, one after neo-adjuvant chemotherapy. Advanced disease was the cause of unresectability in 95 cases. One of three patients with local disease had pulmonary functions allowing the warranted resection. N_2 disease with T_{1-3} on CT scan was found in 47. Three of these patients underwent mediastinoscopy and all confirmed uninvolved N_2. Conclusions: Lung resection rates in our center remain low. Late presentation leading to advanced disease and poor pulmonary reserves preclude resection in most cases. More liberal use of mediastinal staging and better assessment of pulmonary functions may allow us to improve resection rates.

Keywords: Lung cancer - mediastinoscopy - pulmonary functions - resection

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Introduction

Operative treatment of lung cancer has been available and ever improving since Graham and Singer did the first pneumonectomy for lung cancer in 1933 (Graham et al., 1993). Higher resection rates have been associated with better survival (Riaz et al., 2012; Khakwani et al., 2013). Despite efforts at screening, fast tract investigation and treatment of lung cancer; the resection rates for lung cancer worldwide are not high (Damhuis et al., 1995). The reported rates of lung cancer resection stands around 25% in the United States (Dransfield et al., 2006) and 20% in Europe (Coleman et al., 2011). Studies carried out in the U.K. found in 1990's the resection rates in Great Britain to be around 10%, far less than the average of the western Europe (Damhuis et al., 1995).

Advanced stage at presentation has been universally identified as the main cause of low resection rates. In industrialized countries with high literacy rates and high levels of awareness, factors like availability of cancer services near one's residence and travel times to avail these services, the type of hospital (teaching Vs non teaching) have been found to impact on stage of presentation and therefore resection rates (Crawford et al., 2009; Wouters et al., 2010). In countries like ours this trend of late presentation, advanced stage at presentation and therefore poor resectability rates are thought to be directly linked to ignorance, illiteracy and lack of appropriate health services.

Although it is known that the rates of Lung Cancer resection in Nepal are far below the international standards and this state of affairs is blamed on the patient for presenting late, the reasons for low resection rates in our population has not been studied. In this study we tried to determine the delays and other factors that lead to poor resection rates. The attempt was to try and identify the steps through which the patients passed before he/she finally arrived to specialist care at Manmohan Cardio-Thoracic Vascular and Transplant Center (MCVTC) and also determine the time lost in each step.

Materials and Methods

This cross sectional study was conducted in the Thoracic Surgery Unit of the Department of Cardio-Thoracic Vascular Surgery, Institute of Medicine, Tribhuvan University. Hundred consecutive patients with lung cancer who presented to MCVTC thoracic surgery services between October 2011 to October 2012 were included. With the help of a standardized proforma, data

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inclusive of the demography, smoking history (pack yrs) and the chief presenting symptom were recorded. The following time periods were defined and recorded:

T_1=Time since the onset of symptoms to assessment at MCVTC

T_2=Time since first contact with a doctor to assessment at MCVTC

T_3=Time since referral to MCVTC with suspicion of Lung Cancer

D_1=Time from onset of symptoms to first contact with a doctor (T_1-T_2) or patient delay

D_2=Time from first contact with doctor to referral to MCVTC (T_2-T_3) or doctor delay

The CT scan staging, the assessment of performance score (PS) and the pulmonary function test (PFT) results when done were also recorded. Based on the assessment of the CT scan, patient's physiological status and respiratory functions an objective assessment of the resectability/ operability was done. Whether or not the particular patient was resectable was stated with justification of the cause of inoperability.

Results

Using non probability consecutive sampling method we enrolled 100 patients with histology proven Lung Cancer between October 2011 and October 2012. Among the 100 patients studied, the mean age was 63.4±8.3 years. Sixth and seventh decades were the commonest age group. M:F was 2:1. There were five patients who denied active smoking but three of them did give history of passive smoking through their spouses. The average number of pack years was 29.2±14.2 (0-63). Two-thirds of these patients were from within the Kathmandu valley. Cough, hemoptysis and chest pain were the commonest symptoms being present in 60% of the patients. General physicians were the commonest source of referral of these patients (n=47) followed by respiratory physicians and oncologists (n=15 each)

Table 1. Patient Demographics

Variable		Number	Percentage
Gender	Male	64	
	Female	36	
Type of cancer	NSCLC	93	
	SCLC	7	
Stage	I	1	1
	II	5	5.3
	IIIA	46	49.4
	IIIB	22	23.6
	IV	19	20.4
	SCLC-limited	0	0
	SCLC-extensive	7	7

The duration of symptoms at the time of assessment at MCVTC (T_1) ranged from 1 week to 36 months (avg.=4.2±1.9 months). The time from the first contact with a doctor to assessment at MCVTC (T_2) ranged from 1 week to 33 months (avg.=1.993±0.68 months). The average time from referral by a doctor to assessment at MCVTC (T_3) was 7 days ranging from 1 to 120 days. Time between the onset of symptoms and first contact with a doctor (D_1) ranged from 7 days to as high as 36 months (avg.=2.325±1.388 months). Fifty four of the patients however did see a doctor within one month. Time elapsed between first contact with a doctor to actual referral with a diagnosis/ suspicion of Lung Cancer (D_2) ranged from 1 day to upto 12 months (avg.= 50.432±65.657 days). When we compared patients coming from within Kathmandu to those who came from outside the valley, we found no difference between D_1 of the two cohorts (1.701±0.790 versus 2.549 months±5.707, p=0.3985). However, the D_2 among those who came from within the valley was significantly shorter than those who came from outside (46.600±11.999 versus 57.114±12.406 months, p=0.023). There was however no difference in the stage of presentation of these two groups with 31/35 (88.5%) of those from outside and 63/65 (96%) from within the valley presenting with locally advanced or metastatic disease.

Assessment of the CT scan showed that only three patients had presented as local disease. The disease was locally advanced in 76 patients and identifiable metastasis was evident in 21. Stages IIIA (n=48) and IIIB (n=25) were the commonest stages at presentation. In this cohort of 100 patients, only three underwent resection. Two patients with local disease were deemed inoperable because of poor performance score (n=1) and inadequate pulmonary reserve to allow the indicated resection (n=1). The two other patients who underwent successful resection of their Lung Cancers included patients with locally advanced but resectable disease. One patient underwent Right Upper lobectomy with chest wall resection for $T_3N_0M_0$ lesion and another patient underwent resection post neo-adjuvant chemotherapy. Among patients with locally advanced disease, 66/76 (86.84%) patients were found to have poor PFT which could have precluded indicated resection even if the stage was lower. Among patients with T_{1-3} lesions, we found 47 patients with N_2 nodes on CT scan. These patients would have been potentially resectable if the nodes were to be found to be non-cancerous. Only three of these patients had the PFT/PS to allow resection. These patients underwent mediastinoscopy and all were proven on histology to have uninvolved N_2. Two of these patients underwent resection but one did not follow up after mediastinoscopy.

Only three patients ultimately underwent resection. The reasons for unresectability being advanced disease

Table 2. Summary of Time Delays for Each Time Period

Time period	Delay
T_1= Time since the onset of symptoms to assessment at MCVTC	4.264±5.905 months;Range-0.25 to 36 months
T_2=Time since first contact with a doctor to assessment at MCVTC	1.993±1.689 months; Range-0.1 to 33 months
T_3=Time since referral (with suspicion of Lung Cancer) to assessment at MCVTC	8.036±2.137 days; Range-0-120 days
D_1=Time from onset of symptoms to first contact with a doctor (T_1-T_2) or patient delay	2.325±5.388 months; Range-0-35.66 months
D_2=Time from first contact with doctor to referral to MCVTC (T_2-T_3) or doctor delay	50.432±5.657 days; Range-0-365 days

and/or inadequate respiratory reserve and/or poor performance score in 95. Poor Pulmonary functions and performance scores were the cause in otherwise resectable disease in two.

Discussion

Lung Cancer being the overall commonest cancer among the Nepalese population, represents a huge disease burden. In 1997, we reported a resection rate of 5.23% in a series of 527 lung cancers (Sayami et al., 1997) Although there is paucity of data, it is clear that resection rates haven't gone far ahead. Although resection rates in our cohort was only 3%, it certainly cannot be generalized. A larger study encompassing other centers who provide care to lung cancer patients will be needed to actually determine resection rates in the country. However, this is not the objective of the present study. Our study identified significant delays in almost all steps of lung cancer identification.

Ellis (Ellis et al., 2011) reported from Canada and concluded "Lung cancer patients experience substantial delays from development of symptoms to first initiating treatment. There is a need to promote awareness of lung cancer symptoms and develop and evaluate rapid assessment clinics for patients with suspected lung cancers." The median total waiting time in their study was approximately 4.5 months. This is despite Canadian Strategy for Cancer Control recommendation that the maximum time to diagnose most cancers should not exceed four weeks. Jensen (Jensen et al., 2002) showed that the time intervals between first symptom and contacting a doctor varied widely from a median of 7 days to 6 months. Delays that occurred in the assessment in western countries varied widely from 48 to 189 days (Bozcuk et al., 2001). In a UK regional study (Billing et al., 1996) showed that the mean total delay from presentation to operation for Non Small Cell Lung Cancer (NSCLC) was 109 days. Rich (Rich et al., 2011) also from UK found that resection rates and subsequently survival data were better when patients had easier access to thoracic surgical facilities. In India where conditions are not very different from ours, Chandra (Chandra et al., 2009) found the median symptom to initiation delay to be 185 days. They found that this time was significantly longer in patients who had been put on anti- tubercular therapy (ATT) on empirical basis before the diagnosis of lung cancer. In our study the average time from initiation of symptoms to first contact with a doctor was 4.3 months and another 2 months on average were lost before the patients were referred with a suspicion/diagnosis of lung cancer. This delay in recognition of lung cancer reflects the lack of awareness, lack of access to appropriate medical facilities and low level of suspicion among doctors who see these patients first. These are modifiable factors and efforts towards improving them are likely to be beneficial in the effort to diagnose more resectable lung cancers but the process is likely to be tedious and slow.

Studies have been conducted to see if these delays (both patient related-D_1 and doctor/hospital related-D_2) have an impact on the outcome of lung cancer patients. The study by Myrdal et al suggests that increased delay has no negative influence on survival (Myrdal et al., 2004). This has been attributed to the fact that because lung cancer usually only becomes symptomatic in late stages, delays that occur after patient becomes symptomatic will not influence patient outcome except in the very few who have large but still potentially resectable tumour (Billing et al., 1996; Myrdal et al., 2004). This has been the argument used to drive the screening for lung cancer which has shown promising results with low dose CT scan. This however would be difficult to apply in countries like Nepal. Increasing awareness about Lung Cancer symptoms among general public and encouraging more aggressive investigations in smokers with symptoms seems to be the best strategy in developing countries (Chandra et al., 2009).

Poor pulmonary function was also found to be a major factor limiting the resectability rates in our patients. The pulmonary assessment was done by routine spirometry. However, normal spirometry values may vary, and interpretation of results relies on the parameters used. The normal ranges for spirometry values vary depending on the patient's height, weight, age, sex, and racial or ethnic background (Margolis et al., 1997; Petty et al., 2001). Also, parameters in patients with mild disease can overlap with values in healthy persons (Crapo et al., 1989). Studies have shown that pre-operative pulmonary function assessment based on FEV_1 could result in an overly restrictive approach to surgical therapy (Win et al., 2005.) A number of studies indicate that the maximum oxygen uptake (as a percent of predicted), determined by cardiopulmonary exercise testing, is better than spirometry for predicting postsurgical complications (Olsen et al., 1989). However facilities for these tests being unavailable in our center, it is possible that we might be underestimating pulmonary functions of patients who would otherwise be considered for more aggressive therapy. This may be contributing to our low resection rates.

Our assessment of the Nodal stage (mediastinal lymphadenopathy) was based primarily on CT scan with a node with short diameter ≥1cm being considered positive. However, it has been known for a while that CT mediastinal assessment based on node size is not accurate even when the cutoff size is taken at 20 mm (Kerr et al., 1992). Also fifteen percent of lymphnodes less than 10mm were found to be harbouring metastasis (Kerr et al., 1992). Forty seven patients in our study had N_2 T_{1-3} by CT scan. In the absence of invasive mediastinal staging it is very much possible that we may have been overstaging the N stage and thus contributing to low resection rates. This inference is also supported by the finding that all the patients who had enlarged mediastinal nodes on CT scan and subsequently underwent mediastinoscopy were found to have uninvolved nodes.

This is a single center study and the number of patients is small. it is not possible to generalize our findings. A larger multi- center study will be needed to elaborate and validate the issues identified in our study.

In conclusion, our study clearly demomstrates appauling delays in every step of diagnosis and referral of lung cancer patients. The resultant advanced stage

at presentation no doubt contributes to the observed very low resection rates. However, in the absence of appropriate tools of assessment of nodal staging and pulmonary functions, it is possible that we are missing some potentially resectable cases. Routine use of mediastinoscopy and better pulmonary function assessment may help improve our resection rates.

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