

A descriptive analysis of lung and pleural tumours in a premier referral centre in Sri Lanka

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Abstract

Introduction

This study describes pathological findings of lung and pleural neoplasms among a cohort of Sri Lankan patients.

Methods

A descriptive cross-sectional study was conducted among patients with lung and pleural tumours referred to National Hospital for Respiratory Diseases in 2017. Patients who underwent biopsy under direct vision or radiological guidance were included. Contrast Enhanced Computerized Tomography (CECT) findings were correlated with the histological diagnosis.

Results

The population was aged 8-93 [mean (SD)=58.4(13.3)] years. Of 396 patients, 252(63.6%) were males. Majority (n=324, 81.4%) had lung tumours while 72(18.2%) had pleural tumours. Malignant neoplasms were found in 373(n=94.2). Of them, majority (n=180, 45.5%) were core biopsies, followed by lobectomies (n=77, 19.4%). Commonest benign lung tumour was hamartoma (n=13, 3.3%). Schwannoma was the commonest benign pleural tumour (n=3, 0.8%). Among the primary malignant lung tumours, adenocarcinoma was the commonest (n=124, 31.3%). Six (1.5%) primary malignant pleural neoplasms (mesotheliomas) were found. Among the metastatic deposits in the lung, the majority was colorectal adenocarcinomas (n=9, 2.3%). The sensitivity, specificity, positive and negative predictive values of CECT in discriminating malignant lung and pleural tumours were 94.6%, 90.9%, 99.3%, and 54.1% respectively. A one-way ANOVA showed significant differences in the distribution of age among different types of masses [F (5,396) =2.759, p=.018]. The age of patients with benign lung neoplasms (mean=51.3±17.4 years), was less compared to the malignant pleural tumours and primary malignant lung tumours.

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Primary malignant lung tumours predominated among males [χ^2 (5,396) =27.463, p=.000].

Conclusions

Adenocarcinoma was the commonest primary lung tumour (Male: Female=1.6:1). There was a male predominance in primary malignant lung tumours. CECT has a poor negative predictive value in discriminating malignant neoplasms of lung and pleura.

Introduction

The spectrum of lung and pleural neoplasms include benign and malignant tumours, while the latter can be further subcategorized into primary and secondary (metastatic) lung malignancies. The lung is considered the most common organ of the body to be involved by metastatic tumours (1). Age standardized incidence of lung cancer continues to increase by 0.1% per year in males and 0.3% per year in females (2). It is projected to be the second leading cancer in men in 2030 (3). Similarly, the incidence and mortality of lung cancer have risen exponentially in the Asian region (4). According to published data, lung cancer is responsible for the most common cancer related mortality in Sri Lanka (1.38% of total deaths) (5) and accounts for the second highest direct healthcare cost caused by smoking in the country in the year 2017 (6). Even though pleural neoplasms are relatively uncommon compared to the malignancies involving the lung, the associated high morbidity and mortality warrants timely diagnosis and proper management of these lesions (7).

Being an island, Sri Lanka has a relatively different pool of genes compared to the rest of the world. Similarly, socioeconomic and cultural differences lead to the exposure of different types of risk factors for lung and pleural neoplasms in this country. Hence, it is sensible to hypothesize that the clinicopathological and demographic characteristics of lung and pleural neoplasms may differ in Sri Lanka from the rest of the world. Nevertheless, studies on socio-demographic factors, clinicopathological findings and radiological correlations related to lung and pleural tumours are sparse in Sri Lanka. These data are imperative to devise screening strategies and to assess the diagnostic yield of each investigation modality.

National Hospital for Respiratory Diseases (NHRD), Welisara is the premier referral centre for patients with lung and pleural tumours in Sri Lanka. Hence, a nationally representative sample could be obtained from this hospital. Therefore, this study describes the socio-demographic and pathological findings of lung and pleural tumours among Sri Lankans in the year of 2017 who were referred to the NHRD. We also intended to assess the sensitivity, specificity, positive and negative predictive values of computed tomography and cytology in diagnosing lung and pleural lesions.

Methods

This descriptive cross-sectional study was conducted at the NHRD from 1st January to 31st December 2017. The study protocol conformed to the guidelines of the Declaration of the Helsinki (8) and the approval was obtained by the participating institution.

All the patients diagnosed with lung and pleural tumours by means of histopathological analysis in the institution were included in the study. If the patients underwent serial biopsies (eg: patients who had a core biopsy and subsequently underwent lobectomy or pneumonectomy), the most recent biopsy was analysed to prevent duplication of results. There were no particular exclusion criteria. Socio-demographic details of the subjects (age, gender, nationality and comorbidities), procedural details, operative findings and pre-procedural Contrast Enhanced Computed Tomography (CECT) findings were collected. Standard histological stains and immunohistochemical stains were used and specimens were analysed by a consultant pathologist. Pre-procedural CECT films were analysed by a consultant radiologist. If there was radiological evidence or suspicion of a malignancy, the CECT was categorized as “malignant”. If none of the features was suggestive of a malignant neoplasm, the CECT was categorized as “benign”. Patients with at least a single positive biopsy result for malignant cytology or histology of the lung or pleura and radiological evidence of multiple metastasis were considered as patients with multiple metastasis. Data were analysed using Statistical Package for Social Sciences (SPSS) software, version 23. Descriptive data were presented as percentages or as mean \pm standard deviations. Significance of associations among continuous variables was tested using a one-way Analysis of Variance (ANOVA) and independent sample t-test, and categorical variables using a chi-squared test. In all analyses, a p-value ≤ 0.05 was considered statistically significant.

Results

Socio-demographic characteristics

The study sample size was 396; of those, 252 (63.6%) were males and 144 (36.4%) were females. The population was aged 8-93 [mean (SD) = 58.4 (\pm 13.3)] years. Of them, 73

were previously diagnosed with a malignancy. The sample comprised of 324 (81.4%) patients with lung tumours and 72 (18.2%) patients with pleural tumours. The majority (n=59, 14.9%) of the lung tumours originated from the left upper lobe. The majority (n=61, 15.4%) of the pleural tumours involved the right pleura. A summary of the sites of the tumours is given in Table 1. In our study 373 (n=94.2) were malignant tumours. A minority (n=23, 5.8%) was benign. Biopsies were obtained under radiologically guided or operative techniques (eg: bronchoscopy, thoracoscopy). Of the malignant tumours, majority (n=180, 45.5%) were core biopsies, followed by lobectomies (n=77, 19.4%). All the pleural biopsies (n=72, 18.2%) were obtained from Video Assisted Thoracoscopic Surgeries (VATS). A summary of the sampling methods is given in Table 2.

Histological findings

Hamartoma was the commonest benign lung tumour (n=13, 3.3%). Schwannoma was the commonest benign pleural tumour (n=3, 0.8%). Among the primary malignant lung tumours, adenocarcinoma was the commonest (n=124,

Table 1. Distribution of the main primary sites of the lung and pleural tumours

Site of the tumour	Number (percentage)
Right upper lobe	57 (14.4%)
Right middle lobe	21 (5.3%)
Right lower lobe	58 (14.6%)
Left upper lobe	59 (14.9%)
Left lower lobe	46 (11.6%)
Right main bronchus	3 (0.8%)
Left main bronchus	4 (1.0%)
Lower trachea	1 (0.3%)
Right pleura	61 (15.4%)
Left pleura	55 (13.9%)
Multiple lobes of lung	31 (7.8%)

Table 2. Distribution of the main primary sites of the lung and pleural tumours

Site of the Tumour	Biopsy method	Frequency (Percentage)
Lung Tumours	Core biopsy	180 (45.5%)
	Lobectomy	77 (19.4%)
	Pneumonectomy	10 (2.5%)
	Segmentectomy	2 (0.5%)
	Wedge resection	21 (5.3%)
	Excision biopsy	34 (8.6%)
Pleural Tumours	VATS	72 (18.2%)

31.3%). Of them, 117 (29.5%) were differentiated. This was followed by 89 (22.5%) squamous cell carcinomas of the lung. The majority of them were well differentiated squamous cell carcinomas (n=64, 16.2%). Overall there were 17 patients with small cell carcinoma and 258 patients with non-small cell carcinoma. Of 396 study participants, six primary malignant pleural neoplasms (mesotheliomas) were found. Among the metastatic deposits in the lungs from extrapulmonary malignant tumours, the majority was from colorectal adenocarcinomas (n=9) followed by sarcomas (n=8). Primary lung adenocarcinoma was the commonest cause of secondary pleural deposits (n=21) from primary malignant lung tumours. Table 3 summarizes the histological categories of tumours with the age at presentation. The distribution of the lung and pleural neoplasms according to the histological findings are summarized in Table 4. Previous cytology (bronchial brush or wash, fine needle aspiration) reports were available in 51 patients. Forty-seven patients with previous cytology reports had malignant neoplasms confirmed by histological examination. Of them, four cytology reports were concluded as benign and one report was inconclusive. A summary of previous cytology and histological findings of benign and malignant neoplasms is given in Table 5. The sensitivity and specificity of cytology in detecting malignant lung and pleural tumours were 89.4% and 75.0% respectively in this study. The positive predictive value of cytology to detect malignant tumour was 97.7%, and the negative predictive value was 37.5%.

Radiological findings

CECT was obtained prior to the surgery or endoscopy in 338 (85.4%) patients. Out of 316 patients with malignant tumours who underwent CECT, 299 (94.6%) were detected as suspicious for a malignant lesion in CECT. Of the malignant tumours, 17 (5.4%) were categorized as non-suspicious in CT. Four adenocarcinomas of the lung were interpreted as lung abscesses in the CT scans by the radiologist. A summary of the CT and histological findings of benign and malignant neoplasms are given in Table 6. Thus, the sensitivity and specificity of CECT in detecting malignant lung and pleural tumours were 94.6% and 90.9% respectively in this study. The positive predictive value of CECT to detect malignant tumour was 99.3%, and the negative predictive value was 54.1%.

Results of the statistical analysis

A one-way Analysis of Variance (ANOVA) was used to examine whether the presenting age differs with respect to the histological type of the neoplasm. The independent variables included benign and malignant lung and pleural neoplasms. The malignant neoplasms were further categorized as primary and secondary. The dependent variable was the average age of

Table 3. Age at presentation in different categories of lung and pleural neoplasms. (SD=standard deviation).

Category of tumour	Number (Total)	Age at presentation (years)	
		Mean \pm SD	Range
Benign lung neoplasms	17 / 396	51.3 \pm 17.4	9.5 – 71.0
Benign pleural neoplasms	6 / 396	54.1 \pm 16.7	24.0 – 73.0
Primary malignant lung neoplasms	275 / 396	59.0 \pm 12.4	14.0 – 89.0
Primary malignant pleural neoplasms	6 / 396	61.2 \pm 6.9	49.0 – 70.0
Secondary malignant lung neoplasms	32 / 396	52.9 \pm 15.7	14.0 – 74.0
Secondary malignant pleural neoplasms	60 / 396	60.0 \pm 14.0	8.0 – 93.0

the patient at presentation. Means and standard deviations of the age at presentation of different categories are given in Table 3. The test for normality, examining standardized skewness and the Shapiro-Wilks test, indicated the data were statistically normal. The Levene's F test revealed that the homogeneity of variance assumption was met ($p=1.7$). An alpha level of .05 was used for all subsequent analyses. The one-way between groups ANOVA revealed a statistically significant main effect, $F(5,396) = 2.759$, $p=.018$, indicating that the age at presentation significantly differs among histological types of lung and pleural neoplasms. Post-hoc comparisons using the LSD test showed that the age of patients with benign lung neoplasms (mean = 51.3 \pm 17.4 years), was less compared to the malignant pleural tumours and primary malignant lung tumours (Table 3). An independent sample t-test was conducted to compare the age at presentation between small cell and non-small cell lung tumours. There was no significant difference between small cell cancers ($M=57.9$, $SD=12.3$ years), and non-small cell cancers ($M=59.1$, $SD=12.4$ years); $t(273) = -0.394$, $p=0.694$. A Chi-square test for independence indicated a significant association between gender and the type of lung tumour, [$\chi^2(5,396) = 27.463$, $p=.000$]. Figure 1 describes the distribution of lung and pleural neoplasms categorized according to gender. Primary malignant lung tumours were common among males compared to females (Figure 1).

Discussion

Histopathological classification of lung and pleural neoplasms is complex due to tumour heterogeneity and histological diversity (9). Even though examining tumour morphology under haematoxylin and eosin stain is adequate to diagnose most of these tumours, recent advancements of

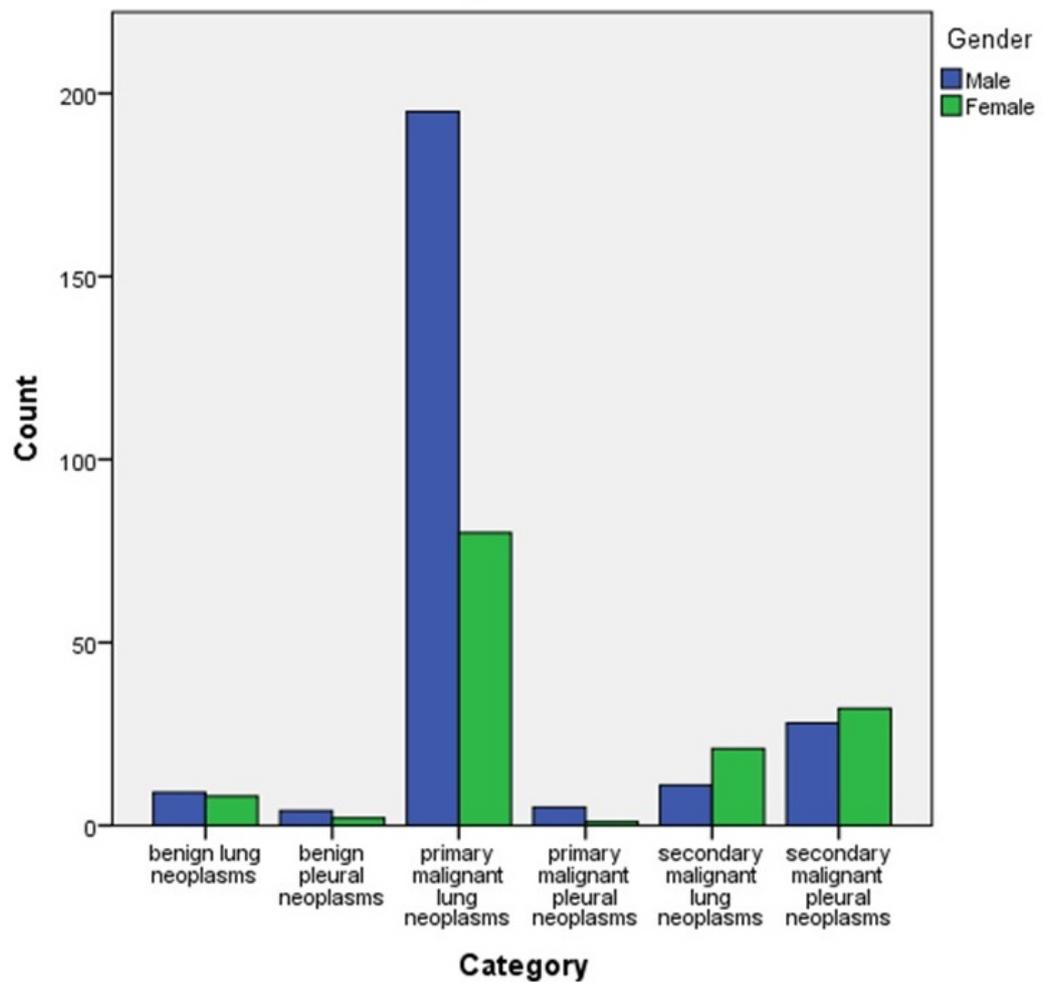


Figure 1. Primary malignant lung tumours compared among males to females

immunohistochemistry have facilitated accurate diagnosis of these neoplasms (9). However, late presentation of these malignancies has led to the poor prognosis of malignant pleural and lung neoplasms. There is no proper screening programme for lung and pleural malignancies in Sri Lanka to date. Hence, a high degree of clinical suspicion with a proper radiological and histopathological evaluation is essential for better outcomes.

Malignant lung and pleural neoplasms are commonly seen among the elderly (10). Secondaries are reported to be commoner in the lung compared to the primary neoplasms (9). However, in our study, we found that 89.6% of the lung malignancies were primary, whereas only 10.4% accounted for the metastatic neoplasms. The reason for this would be that the patients with advanced metastatic neoplasms are commonly treated at the National Cancer Institute Maharagama (Apeksha Hospital) and are not referred to as NHRD. Among the metastatic tumours of the lung, the commonest to be reported worldwide is adenocarcinoma (11). Considering metastatic lung malignancies reported in our study, colorectal adenocarcinoma (n=9) and soft tissue

sarcoma (n=8) were the commonest extrapulmonary malignant tumours. According to a joint point regression of the cancer registries in the United States, the commonest histopathological type of primary lung malignancy was adenocarcinoma (11). Similarly, in our study, the most common histopathological variant of primary lung malignancy was adenocarcinoma (n=124) followed by squamous cell carcinoma (n=89). Hamartoma was the most frequent benign lung tumour in our study accounting for 76% (n=13) of the benign neoplasms of the lung. Correspondingly, Hamartomas were consistently found to be the most prevalent benign lung tumour in the west (12, 13). Malignant pleural tumours are a less common entity (12). However, when both primary and secondary malignant tumours were taken together, they were commoner than benign pleural tumours (12) which was in accordance with our study. Adenocarcinoma is the commonest histological type of the pleural secondaries worldwide (12). Similarly, breast and lung adenocarcinomas were the commonest pleural secondaries found in our study.

Smoking is one of the major modifiable risk factors for lung

Table 4. Distribution of histopathological types of lung and pleural tumours in the study population.

Category of tumour	Site of Tumour	Type of Tumour	Frequency (Percentage) out of 396 study participants (N=396)	Gender		Age (years)		
				Male	Female	Mean \pm SD	Range	
Benign	Lung	Adenoma	1 (0.3%)	1	0	50	-	
		Congenital Pulmonary Airway Malformation	3 (0.8%)	1	2	27.5 \pm 20.0	9.5 – 49.0	
		Hamartoma	13 (3.3%)	7	6	56.8 \pm 12.7	29.0 – 71.0	
	Pleura	Spindle cell tumour	1 (0.3%)	0	1	62.0	-	
		Schwannoma	3 (0.8%)	3	0	55.5 \pm 5.5	49.0 – 59.0	
		Neurofibroma	2 (0.5%)	1	1	48.5 \pm 34.6	24.0 – 73.0	
Malignant (Secondary)	Lung	Adenoid Cystic Carcinoma	1 (0.3%)	1	0	41.0	-	
		Breast adenocarcinoma	5 (1.3%)	1	4	58.2 \pm 11.1	41.0 – 69.0	
		Malignant notocordal tumour (Chondroid Chordoma)	1 (0.3%)	1	0	73.0	-	
			Colorectal adenocarcinoma	9 (2.3%)	2	7	56.0 \pm 10.1	41.0 – 68.0
			Malignant thymoma	1 (0.3%)	0	1	57.0	-
			Ovarian adenocarcinoma	2 (0.5%)	0	2	58.5 \pm 4.9	55.0 – 62.0
			Parotid carcinoma	1 (0.3%)	1	0	50.0	-
			Renal cell carcinoma	2 (0.5%)	1	1	65.5 \pm 12.7	56.0 – 74.0
			Sarcoma	3 (0.8%)	3	0	42.7 \pm 30.0	8.0 – 60.0
			Thymoma	3 (0.8%)	1	2	70.3 \pm 7.6	65.0 – 79.0
			Thyroid follicular carcinoma	1 (0.3%)	1	0	69.0	-
	Malignant (Primary)	Lung	Adenocarcinoma (differentiated)	117 (29.5%)	72	45	61.3 \pm 10.8	33.0 – 89.0
			Adenocarcinoma (poorly differentiated)	7 (1.8%)	6	1	58.1 \pm 10.7	47.0 – 75.0
Neuroendocrine (atypical carcinoid tumour)			6 (1.5%)	2	4	43.0 \pm 10.5	31.0 – 57.0	

		Neuroendocrine (large cell tumour)	2 (0.5%)	2	0	49.0 ± 7.1	44.0 – 54.0
		Miscellaneous (adenoid cystic carcinoma)	4 (1.0%)	1	3	48.3 ± 11.0	35.0 – 60.0
		Miscellaneous (Large cell carcinoma)	2 (0.5%)	1	1	57.5 ± 4.9	54.0 – 61.0
		Miscellaneous (lymphoma)	1 (0.3%)	0	1	30.0	-
		Miscellaneous (osteoclastoma)	1 (0.3%)	1	0	41.0	-
		Miscellaneous (round cell tumour)	2 (0.5%)	1	1	43.5 ± 7.8	38.0 – 49.0
		Miscellaneous (sarcoma)	9 (2.3%)	5	4	51.2 ± 19.8	16.0 – 73.0
		Miscellaneous (spindle cell carcinoma)	1 (0.3%)	0	1	60.0	-
		Small cell carcinoma	17 (4.3%)	13	4	57.9 ± 12.3	31.0 – 77.0
		Squamous cell carcinoma (differentiated)	64 (16.2%)	59	5	62.6 ± 9.5	36.0 – 84.0
		Squamous cell carcinoma (poorly differentiated)	25 (6.3%)	24	1	61.8 ± 11.8	14.0 – 75.0
Malignant (primary)	Pleural	Mesothelioma	6 (1.5%)	5	1	61.2 ± 6.9	49.0 – 70.0

Table 5. Cross tabulation of histologically confirmed benign and malignant neoplasms against the cytology finding prior to obtaining histology

		Histological finding	
		Malignant	Benign
Cytology finding	Malignant	299	2
	Benign	17	20

Table 6. Cross tabulation of histologically confirmed benign and malignant neoplasms against the Computed Tomography (CT) finding prior to obtaining histology

		Histological finding	
		Malignant	Benign
Computed Tomography finding	Malignant	299	2
	Benign	17	20

cancer worldwide (14, 15). A systematic review showed that the recent changes in the trends of smoking are reflected in the prevalence of lung cancer morbidity and mortality (16). In a Sri Lankan study, smoking was found to be more prevalent among men than in women (17). This is the most likely reason for primary lung neoplasms to be 2.4 times commoner in males than females in our study population.

CECT of the chest plays a major role in diagnosing, radiological staging and assessment of resectability of lung tumours. Common radiological findings of pleural neoplasms include effusions, pleural thickening and plaques (12). Characteristics of the lesion, involvement of fissures and lobes, ipsilateral and contralateral lung metastasis, involvement of pulmonary artery, vein and mediastinal lymph nodes are considered in radiological staging and assessing the resectability of malignant tumours (18). A study conducted by Dabrowska et al concluded that CECT had high sensitivity and a negative predictive value in identifying malignant

solitary pulmonary nodules (19). In our population, the sensitivity (94.6%) and specificity (90.9%) of CECT chest in diagnosing malignant lung and pleural tumours were high. However, CECT had a low negative predictive value of 54.1%.

Conclusions

Adenocarcinoma was the commonest primary lung tumour reported in the study population (Male: Female=1.6:1). There was a male predominance in primary malignant lung tumours. Adenocarcinoma was the commonest malignancy in males. CECT had a poor negative predictive value in discriminating malignant neoplasms of lung and pleura. Further studies with large numbers are needed to identify the patterns of socio-demographic and pathological characteristics associated with lung and pleural neoplasms in Sri Lanka.

All authors disclose no conflict of interest. The study was conducted in accordance with the ethical standards of the relevant institutional or national ethics committee and the Helsinki Declaration of 1975, as revised in 2000.

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