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Original Research Article

Screening COPD (Chronic Obstructive Pulmonary Disease) Patients for lung Cancer

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ABSTRACT

Introduction: Patients with chronic obstructive pulmonary disease (COPD) are at increased risk for both the development of primary lung cancer, as well as poor outcome after lung cancer diagnosis and treatment. The present study was undertaken to screen COPD patients for lung cancer and to find clinical and laboratory correlates of lung cancer in patients of COPD.

Material and Methods: The present hospital based study comprised of 200 consecutive patients suffering with COPD. The patients were subjected to chest – radiography (both posteroanterior and lateral views), sputum cytology, fibre optic bronchoscopy and high resolution computed tomography (HRCT). Data was analyzed by standard statistical procedure using descriptive statistics method and comparisons were made by using chi-square test, and odds ratio. A 'p' value of < 0.05 was taken as statistically significant.

Results: Among the various screening modalities used in this study, sputum cytology provided the lowest sensitivity (33.33%) and specificity (67.67%) while HRCT chest afforded the best sensitivity (91.7%) and specificity (95.7%). The variables significantly associated with lung cancer in our study were smoking, anorexia, anemia, weight loss, clubbing, and indices of lung function tests.

Conclusion: In conclusion, patients with COPD constitute a group at high risk for lung cancer. Screening these patients, particularly those with increasing severity of obstruction is worthwhile in as much as it has the promise of early detection and consequently early treatment and improved survival. Chest CT appears to be the best screening procedure given its excellent sensitivity and specificity.

Keywords: Chronic obstructive pulmonary disease; Lung Carcinoma; Chest CT.

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INTRODUCTION

Patients with chronic obstructive pulmonary disease (COPD) are at increased risk for both the development of primary lung cancer, as well as poor outcome after lung cancer diagnosis and treatment.[1] COPD was the third most common cause of death worldwide in 2010 and ranked fifth worldwide in terms of burden of disease.[2] Chronic inflammation associated with COPD likely plays a role in the pathogenesis of lung cancer, just as chronic inflammation contributes to malignant transformation in other organs. Inflammation in COPD may result in repeated airway epithelial injury and accompanying high cell turnover rates and propagation of DNA errors resulting in amplification of the carcinogenic effects of cigarette smoke.[1] Cigarette smoking is an important risk factor for COPD and lung cancer. COPD is an independent risk factor for lung carcinoma, particularly for squamous cell carcinoma[3] and the risk of lung cancer increases up to five times in smokers with airflow obstruction than those with normal lung function.[4] The present study was undertaken to Screen COPD patients for lung cancer and to find clinical and laboratory correlates of lung cancer in patients of COPD.

MATERIAL AND METHODS

The present hospital based study comprised of 200 consecutive patients suffering with COPD enrolled from both outpatient and inpatient (wards) departments at Sher –I – Kashmir Institute of Medical Sciences. An informed consent was obtained from the patients. The study was approved by the Institutional ethical Review Board. The patients included in the study were men and women (both smokers and nonsmokers) aged 40 years or more

with history suggestive of COPD (cough with sputum production in chronic bronchitis and breathlessness in emphysema), physical findings suggestive of airway obstruction (rhonchi, decreased intensity of breath sounds, and prolonged expiration). Patients with radiological evidence of significant lung disease (e.g. pneumonia, heart failure, pulmonary embolism) were excluded from the study. The patients were subjected to chest – radiography (both posteroanterior and lateral views), sputum cytology, fibre optic bronchoscopy and high resolution computed tomography (HRCT).

Statistical Methods: Data was analyzed by standard statistical procedure using descriptive statistics method and comparisons were made by using chi-square test, and odds ratio. A 'p' value of < 0.05 was taken as statistically significant.

OBSERVATIONS

Table 1 shows the clinical details of the patients studied. Expectedly nearly all the patients had cough, expectoration, and breathlessness.

About a half of the patients had breathlessness for 6-10 years at the time of study. Three fourths of the patients had 1-5 exacerbations of COPD in the preceding two years and about two thirds had been admitted to hospital once or twice in the preceding five years.

Two thirds of the patients had abnormal shape of chest; two thirds had abnormal findings on chest auscultation. There was a significant correlation between haemoptysis, number of hospital admissions, weight loss, anorexia, anemia (pallor), clubbing and chest shape with malignancy.

Table 1: Clinical profile and Hospital admissions in Relation to malignancy

Symtom/Sign		Malignancy		OR	p.value
		Present	Absent		
Cough	P	12 (100%)	186(98.9%)		>0.05 (NS)
	A	0 (0)	2 (1.1%)		
Expectoration	P	12 (100%)	171 (91.0%)		> 0.05 (NS)
	A	0 (0)	17 (9.0%)		
BLN	P	11 (91.7%)	175 (93.1%)		> 0.05 (NS)
	A	1 (8.3%)	13 (6.9%)		
Duration of	≤5yr	2 (16.7%)	71 (37.8%)	3.03	> 0.05 (NS)
BLN	>5yr	10 (83.3%)	117 (62.2%)		
Heamoptysis	P	3 (25%)	14 (7.4%)	4.14	<0.05 (Sig)
	A	9 (75%)	174 (92.6%)		
No. of exacerbations	≤5	8 (66.7%)	157 (83.5%)	2.53	>0.05 (NS)
for last 2 yrs	>5	4 (33.3%)	31 (16.5%)		
No. of Hospital admissions	≤ 2	4 (33.3%)	145 (77.1%)	6.74	<0.05 (Sig)
	> 2*	8 (66.7%)	43 (22.9%)		
Wt. loss	P	9 (75.0%)	57 (30.3%)	6.90	<0.05 (sig)
	A	3 (25.0%)	131 (69.7%)	(-1.1-5.6)	
Anorexia	P	9 (75.0%)	84 (44.7%)	3.71	< 0.05 (Sig)
	A	3 (25.0%)	104 (55.3%)	(-0.5-6.2)	
Pallor	P	9 (75.0%)	44 (23.4%)	9.82	<0.05 (sig)
	A	3 (25.0%)	144 (76.6%)	(-1.3-5.4)	
Cyanosis	P	2 (16.7%)	20 (10.6%)	1.68	>0.05 (NS)
	A	10 (83.3%)	168 (89.4%)		
Icterus	P	0(0)	5 (2.7%)		>0.05 (NS)
	A	12 (100%)	183 (97.3%)		
Clubbing	P	10 (83.3%)	15 (8.0%)	57.7	< 0.05 (Sig)
	A	2 (16.7%)	173 (92.0%)		
Flap	P	0(0)	9 (4.8%)		>0.05 (NS)
	A	12(100.0%)	179 (95.2)		
JVP	P	0 (0)	6 (3.2%)		>0.05 (NS)
	A	12 (100.0%)	182 (96.8%)		
LAP	P	1 (8.3%)	4 (2.1%)	4.18	>0.05 (NS)
	A	11 (91.7%)	184 (97.9%)		
Skin changes	P	2 (16.7%)	9 (4.8%)	3.98	>0.05 (NS)
	A	10 (83.3%)	179 (95.2%)		
Breath sounds	Normal	2 (16.7%)	71 (37.8%)	3.03	>0.05 (NS)
	Added sounds	10 (83.3%)	117 (62.2%)		
CVS	NAD	7 (58.3%)	144 (76.6%)	2.34	>0.05 (NS)
	PAH	5 (41.7%)	44 (23.4%)		
Chest shape	Norma	1 (8.3%)	84 (44.7%)	8.8	<0.05 (sig)
	Barrel/flat*	11 (91.7%)	104 (55.3%)		

P=Present, A=Absent, N=Normal, BLN=Breathlessness, LAP=Lymphadenopathy, NAD=No abnormality detected, PAH=Pulmonary artery hypertension.

Table 2: X-Ray chest in relation to malignancy in studied subjects

	Malignancy				
	Present	Absent	Total	OR/X^2	P value
X-Ray	**n=12**	**n=188**	**n =200**		
Normal	3 (25.0%)	131(69.7%)	134(67.0%)	X2=37.086	P=0.000
Indeterminate	3 (25.0%)	49 (26.1%)	52 (26.0%)		(sig)
suspicious	6 (50.0%)	8 (4.3%)	14 (7.0%)		
X-Ray (clubbed)					
Abnormal *	9 (75.0%)	57 (30.3%)	66(33%)	OR=6.989	P<0.05 (sig)
Normal	3 (25.0%	131(69.7%)	134(67%)		

*Includes indeterminate and suspicious

Table 3:.Sputum cytology in the studied patients and in relation to malignancy

	Total	Present	Absent	Results
Sputum cytology				
Normal or slight atypia	194(97.0%)	8 (66.7%)	186(98.9%)	X^2 = 46.275
Moderate to severe atypia	4 (2.0%)	2 (16.7%)	2 (1.1%)	P=0.000 (Sig)
Malignant cell present	2 (1.0%)	2 (16.7%)	0 (0.0)	
Sputum cytology (Clubbed)				
Abnormal	6(3%)	4 (33.3%)	2 (1.1%)	OR= 46.50
Normal	194(97%)	8 (66.7%)	186(98.8%)	p<0.05 (sig)

Table 4: Co-relation between bronchoscopy and lung cancer

		Total n=60		Malignancy			
				Present n=12		Absent n=48	
		N	%	n	%	n	%
Hyperemia	**Present**	26	43.3	12	20.0	14	23.3
	Absent	34	56.7	0	(0.0)	34	56.7
	Total	60	100.0	12	20.0	48	80.0
Secretions	**Present**	33	55.0	12	20.0	21	35.0
	Absent	27	45.0	O	(0.0)	27	45.0
	Total	60	100.0	12	20.0	48	80.0
Luminal pathology	**Present**	13	21.7	10	16.7	3	5.0
	Absent	47	78.3	2	3.3	45	75.0
	Total	60	100.0	12	20.0	48	80.0
P value		**<0.05 (p <0.05= sig.)**					

Chest X-Ray was interpreted as normal in 134(67%), indeterminate in 52(26%), and suspicious in 14(7%) of the patients. Malignancy was detected in 3(2.2%), 3(5.7%), and 6 (42.85%) respectively of the subjects having normal, indeterminate, and suspicious chest X- ray (table 2). Chest X – Ray findings and malignancy were significantly correlated. Chest X-Ray provided a sensitivity of 75% and a specifity of 69.7% for the detection of lung carcinoma giving positive and negative predictive values of 13.63 and 97.76% respectively.

As shown in table 3, sputum cytology revealed normal results or slight atypia in 194, moderate to severe atypia in 4, and malignant cells in 2; overall sputum cytology was abnormal in 6. Among 194 patients with normal findings or slight atypia on sputum cytology, malignancy was detected in 8(4.3%); 2 of the 4 patients with moderate to severe atypia had lung cancer and malignancy was confirmed in both of the patients having malignant cells on sputum cytology. For the detection of lung cancer, sputum cytology was 33.3% sensitive and 98.8% specific.

The results of bronchoscopy (table 4) performed on a total of 60 subjects are shown in table 8.Hyperemia was found in 26 including the 12 patients found to have malignancy in this study. Secretions were found in 33 including the 12 with malignancy. Intraluminal pathology was found in 13 including only 10 of the 12 patients detected to have malignancy in our study. Overall, bronchoscopy detected 10 of the 12 patients documented to have malignancy in our study giving a sensitivity of 83.3%; 45 of the 48 patients not having malignancy had bronchoscopy results negative for malignancy giving this procedures a specifity of 93.8% (table 5). Bronchoalveolar lavage (BAL) revealed malignant cells in 4 of the 12 patients with malignancy (sensitivity 33%);none of the subjects in whom BAL was negative for malignant cells was proved to have malignancy (specifity 100%).

As shown in table 6, CT detected lung cancer in 11 of the 12 subjects with malignancy while only one of the 45 patients with normal CT chest had lung cancer giving this investigation a sensitivity and specifity of 91.7% and 95.7% respectively.

Table 5: Co-relation between Bronchoalveolar lavage(BAL) and lung cancer

	Malignancy		Total	O R	P
	Present	Absent			
Bronchoscopy (for malignancy)					
+ve	10(83.3%)	3 (6.3%)	13	75.00	<0.05(sig)
-ve	2 (16.7%)	45(93.8%)	47		
BAL for Malignant cells					
Present	4 (33.3%)	0 (0.0)	4	45.0	< 0.05(sig)
Absent	8 (66.7%)	45(100.0%)	53		

BAL=Bronchoalveolar lavage

Table 6: Relationship between CT Scan chest and malignancy.

CT Chest	Malignancy				p.value
	Present	Absent	Total	OR	
Normal	1 (8.3%)	44(95.7%)	45		
Mass lesion*	11 (91.7%)	2 (4.3%)	13	242.0	<0.05 sig.
Total	12	46	58		

DISCUSSION

For present study, we used chest X-Ray, sputum cytology, bronchoscopy, and HRCT to screen patients with COPD for lung cancer. Other studies have used these same modalities singly or in various combinations. Bechtal JJ et al[5] used chest X-ray, sputum cytology, and CT chest to screen 88 patients with COPD for lung cancer.

Nearly half (42.85%) of all the patients in whom chest X-Ray was interpreted as suspicious were detected to have lung cancer in our study. The close association between COPD and lung cancer suggests either that there may be common susceptibilities of these diseases to the effects of cigarette smoking or that abnormalities in the COPD lung somehow favor the development of lung cancer beyond the effect of smoking alone.[6]

Out of 194 subjects in whom sputum cytology was normal or showed mild atypia, 4.12% had lung cancer in our study; in contrast lung cancer was found in 2 of 4 with moderate to severe atypia and in both the patients in whom sputum revealed malignant cells. In an earlier study sputum cytology revealed similar results, 95.89, 4, and 0.11% having normal cytology or slight atypia, moderate or more severe atypia, and malignant cells respectively; all 11 patients with malignant cells on sputum cytology and 6 of 14 patients-43%-with marked atypia had lung cancer.[7]

The marginal differences likely stem from a marked difference in sample size in the two studies. The sensitivity of sputum cytology for detection of lung cancer in our study was 33.3% (4 of the 12 cases were detected by sputum cytology which was performed in all the patients). Other studies have reported a sensitivity of 25-49% for this investigation in the detection of lung cancer.[7-9] The difference in the sensitivity reported likely emanate from differences in the sample size and in the yield of sputum for cytological examination in patients with COPD.

In the present study bronchoscopy had a sensitivity of 83.33% and a specificity of 93.8% in the detection of lung cancer. A questionnaire, self-administered in a primary care office setting, helps identify patients at high risk of lung cancer. If upcoming results of randomized controlled trials show a benefit of lung screening, this tool could be of help to select patients for screening.[10]

In 13 of the 58 patients in whom it was obtained, HRCT chest detected lesions in the lung; 11 of these 13 patients had lung malignancy. One of the 12 patients with lung cancer in our study had normal HRCT chest; the cancer in this patient was revealed by bronchoscopy. This gave CT a sensitivity and specificity of 91.7% and 95.7% respectively, which were the highest for any modality in our study.

Swensen SJ et al[11] showed that screening with spiral CT can detect lung cancer at smaller size and earlier stage than can be done with chest radiography; the 92% sensitivity of CT for detecting lung cancer reported by them is similar to that found in our study Thus, CT can detect lung cancer at an early stage and results in increased survival with the consequent early treatment.[12] The clinical characteristics found to be associated with lung cancer in our study were haemoptysis, number of hospital admissions, weight loss, anorexia, anemia, clubbing, and abnormal chest shape.

The limitation of the present study was our inability to perform bronchoscopy and HRCT in all the patients studied that would likely have caused and underestimation of the prevalence of lung cancer in patients screened in this study.

CONCLUSION

Among the various screening modalities used in this study, sputum cytology provided the lowest sensitivity (33.33%) and specificity (67.67%) while HRCT chest afforded the best sensitivity (91.7%) and specificity (95.7%). The variables significantly associated with lung cancer in our study were smoking, anorexia, anemia, weight loss, clubbing, and indices of lung function tests. In conclusion, patients with COPD constitute a group at high risk for lung cancer. Screening these patients, particularly those with increasing severity of obstruction is worthwhile in as much as it has the promise of early detection and consequently early treatment and improved survival. Chest CT appears to be the best screening procedure given its excellent sensitivity and specificity.

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