Original Article

Role of pneumonectomy for lung cancer in current scenario: An Indian perspective

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Abstract

BACKGROUND: Surgical treatment for lung cancer has evolved from pneumonectomy to lobectomy/sleeve resection around the world. Although condemned for poor outcomes, pneumonectomy may still be required in a select group of patients in developing countries. With the better patient selection, optimization of medical comorbidities, better perioperative care; pneumonectomy may show better results. Thus, there is a need to reconsider the role of pneumonectomy in patients with locally advanced lung cancer in the current scenario. **PATIENTS AND METHODS:** The aim of this study was to analyze the demographic and clinicopathologic profile of lung cancer patients and the role of pneumonectomy at a tertiary cancer center in India. The records of patients, who underwent surgery for lung cancer at our institute from January 2011 to April 2014, were analyzed retrospectively, and various parameters in pneumonectomy were compared to lobectomy patients. **RESULTS:** Out of 48 patients undergoing major lung resections, nearly 80% patients were symptomatic at presentation and were mostly in advanced stages, thus requiring neoadjuvant chemotherapy in 45.8% cases and pneumonectomy in 41.6% patients. There was no difference in morbidity and mortality in pneumonectomy (25%, 5%) versus lobectomy (21.2%, 3.5%). Disease-free survival at 1, 2, and 3 years after pneumonectomy (71.8%, 51.4%, and 42.8%) was comparable to lobectomy (73.3%, 66.1%, and 55.6%). After neoadjuvant therapy, survival was not affected by the type of surgery. **CONCLUSIONS:** In the Indian scenario, as the majority of lung cancer patients present at an advanced stage, pneumonectomy still plays a major role, and the acceptable postoperative outcome can be achieved with aggressive perioperative management.

Key Words: Lobectomy, lung cancer, pneumonectomy

Introduction

Lung cancer is a leading cause of cancer-related death in both men and women. Although it accounts for only 15% of all new cancers diagnosed, it leads to more cancer-related death than combined for cancers of the colon, breast, and prostate.[1] Multimodality management with chemotherapy, radiotherapy, and surgery is the current standard of care for treatment of locally advanced lung cancer. As lobectomy is now considered as the standard surgery for lung cancer, the share of pneumonectomy has reduced to 15%.[2] However, the scenario is a bit different in developing countries. Despite significant advances and better availability of facilities for diagnosis and treatment, some factors still hold the developing countries in moving parallel to the rest of the world. Compared to the west, more of our patients tend to present in late stages, mainly due to an initial misdiagnosis as infective processes, especially pulmonary tuberculosis in as many as 14.1% cases. Most patients present in advanced stages; 43% and 70% in Stages III and IV, respectively and, therefore, require induction therapy before definitive surgery.[3,4] This reduces the feasibility of parenchyma-preserving options such as lobectomy, sleeve lobectomy or segmentectomy; which are otherwise less morbid and considered oncologically equivalent to pneumonectomy.[5-7] This brings the need for revisiting the role of pneumonectomy, which was seen to be associated with higher perioperative morbidity and mortality. Though the survival benefit of pneumonectomy, especially after neoadjuvant therapy has been questionable,[8] it may be the only answer for a cure in a select group of patients. In this modern era, where better patient selection and perioperative care have the potential to reduce the surgery-related morbidity, it is imperative to reconsider pneumonectomy as radical but curative treatment option for advanced lung cancer.

The purpose of this study was to evaluate the role of pneumonectomy in the current perspective with respect to the clinical profile of our patients and its clinical and oncological outcomes in patients undergoing surgery for lung cancer at a tertiary care center in India.

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Patients and Methods

We present a retrospective analysis of 48 patients undergoing lung resections (lobectomy, bilobectomy and pneumonectomy, Rajiv Gandhi Cancer Institute Delhi) for lung cancer from January 2011 to April 2014. This was a retrospective study, and clinical data of all patients undergoing major lung resection was collected using electronic data record HIS (VISTA)®. The demographic and clinical details were collected from scanned files. The operative notes, histopathological reports, and postoperative outcomes were recorded and analyzed. Disease-free and overall survivals were calculated from the date of diagnosis to the date of recurrence and death respectively or to the date of last follow-up. Clinical data were analyzed using IBM SPSS Statistics V 22.0. Immediate perioperative outcomes and complications were compared for patients undergoing lobectomy versus pneumonectomy using Chi-square test. Postoperative complications and histopathology reports were analyzed in both the groups. Survival was compared using Kaplan–Meir curve and statistical significance was set at P value of <0.05.

Results

Overall 48 patients underwent lung resection for lung tumors from January 2011 to April 2014. The mean age at presentation was 53.6 years (range 15–77 years), 79.2% were males. Nearly 80% patients presented with symptoms such as cough, hemoptysis, or chest pain; while 8.3% had incidentally detected lung lesions and another 10% had solitary metastatic pulmonary nodules detected during surveillance for cancer at other site [Table 1].

Table 1: Patient characteristics

Variable	Number of patients, *n*=48
Age	
Mean	53.6 years (15-77)
Sex	
Male	38
Female	10
Clinical presentation	
Symptomatic	39
Incidental	4
Surveillance	5
Clinical T stage	
Tx	3
T1a, T1b	2, 7
T2a, T2b	7, 7
T3	21
T4	1
Clinical N stage	
N0	22
N1	12
N2	14
Stage grouping	
Ia, Ib	6, 5
IIa, IIb	4, 6
IIIa, IIIb	19, 3
Metastatic	5
Neoadjuvant therapy	
Chemotherapy	22
Chemoradiation	1
Type of surgery	
Lobectomy	22
Bilobectomy	6
Pneumonectomy	20
Histology	
ADC	16
SCC	20
Others	7
Metastatic	5

Staging according to AJCC 7th ed.ition, 2010. ADC=Adenocarcinoma; SCC=Squamous cell carcinoma; AJCC=American Joint Committee on Cancer

Computed tomography (CT) guided biopsy was done for peripherally placed lesions and fiber optic bronchoscopy and biopsy for centrally located lesions for tissue diagnosis. Whole body 18 fluorodeoxyglucose (FDG^{18}) positron emission tomography (PET) with contrast enhanced CT chest was done for staging workup in all patients and tumor stage grouping was done using International Association for the Study of Lung Cancer modification of American Joint Committee on Cancer seventh edition recommendation. All cases were discussed in tumor board and managed accordingly. Twenty-two patients (46%) were Stage III at the time of diagnosis and 5 (10.4%) were found to be a solitary metastasis from other sites. Twenty-two patients received neoadjuvant chemotherapy for clinical Stage III nonsmall cell lung cancer (NSCLC). Patients with squamous cell carcinoma (SCC) received three cycles of Gemcite/cisplatin while patients with adenocarcinoma (ADC) received 3–6 cycles of cisplatin/paclitaxel/pemetrexed. Postchemotherapy response assessment with FDG^{18} PET CT revealed significant response in 11 patients, partial response in 4 patients and persistent disease in 7 patients. Preoperative workup included routine blood investigations, pulmonary function test (spirometry and diffusing capacity of the lung for carbon monoxide [DLCO]); two-dimensional echocardiography for all patients and stress thallium and ventilation perfusion scan in selected patients.

Twenty-two patients underwent lobectomy, 6 patients underwent bilobectomy, and 20 patients underwent pneumonectomy (right-sided pneumonectomy in 5 and left sided in 15 patients). Systematic mediastinal lymph node sampling was done in all the patients. Four patients had chest wall invasion (involvement of one or more ribs or intercostal muscles) for which *en bloc* resection of the chest wall with reconstructive surgery was done. Preemptive reinforcement of bronchial stump using intercostal/diaphragmatic muscle flap was done in all patients undergoing pneumonectomy after induction therapy.

Patients who underwent pneumonectomy or lobectomy were similar in terms of patient demographics [Table 2]. Seventy-five percent patients undergoing pneumonectomy had Stage IIb/III tumors clinically. Nearly half of these (11/20), received preoperative chemotherapy while one received neoadjuvant chemoradiation. The main indication for pneumonectomy was the presence of a bulky central lesion, fixed anthracotic lymph nodes or extensive posttherapy fibrosis involving the adventitia of vessels. Comparison of immediate postoperative outcomes did not show any difference in total Intensive Care Unit (ICU) and hospital stay for the type of surgery performed (i.e., pneumonectomy or lobectomy). There was no significant difference in the perioperative morbidity or mortality in the two groups. Overall postoperative complications occurred in 25% patients in pneumonectomy and 21.2% patients in lobectomy group. Prolonged air leak and arrhythmia were the most common complication in both groups. One patient in each group developed a broncho-pleural fistula with resultant long-standing empyema that was managed conservatively. There was one perioperative mortality in each group (incidence 5% in pneumonectomy, 3.5% in lobectomy) (P = 0.807) [Table 3]. In patients operated after neo-adjuvant therapy, perioperative mortality was similar to those undergoing upfront surgery and was not significantly different in lobectomy and pneumonectomy.

Final histopathology report revealed ADC in 16 patients (33.3%), SCC in 20 patients (41.7%), poorly differentiated carcinoma and carcinosarcoma in one case each and carcinoid in 4 patients (8.3%). Total lymph node yield was 8.66 in all patients, 12.05 in pneumonectomy specimens and 6.25 in a lobectomy. Histopathologically positive lymph nodes were seen in 7 and 4 patients in pneumonectomy and lobectomy groups respectively. A positive margin was seen in 3 patients in each group (2 bronchial, 1 vascular, 1 visceral pleural and 2 submucosal).

Follow-up data was available for 42 out of 48 patients for survival analysis. Disease-free survivals at 1, 2 and

3 years were 73.3%, 66.1%, and 55.6% in lobectomy group and 71.8%, 51.4% and 42.8% in pneumonectomy group respectively (P = ns) [Figure 1]. Median overall survival was higher in lobectomy group as compared to pneumonectomy (55 months vs. 37 months), respectively, but the difference was not statistically significant. In patients undergoing surgery after neo-adjuvant therapy, median overall survival was 44 months as compared to 55 months in those undergoing upfront surgery (P = ns). After induction therapy, type of surgery did not significantly affect median overall survival, 44 months versus 37 months for lobectomy and pneumonectomy respectively.

Discussion

A major challenge in the management of lung cancer is to improve the overall survival, especially in the developing countries where late presentation curbs the pace of improvement in outcomes that should have been seen with the new techniques. Lobectomy has now become the standard surgical option for lung cancer. More and more patients with early and localized cancers are currently being managed by segmentectomy and sleeve lobectomy resulting in significant reduction in perioperative morbidity and mortality and higher survival rates.[9,10] However, in most series on sleeve lobectomy, only 27.8–30% patients are in clinical Stage III.[9] The clinical stage analysis in our study shows a significantly larger share of locally advanced lung cancer and negates the performance of these parenchyma-preserving surgeries in most of our patients. Moreover, in patients with large sized and centrally located tumors pneumonectomy is more often required to achieve complete resection of disease with negative margins. Pneumonectomy has generally been criticized for its related complications, and, therefore, there has been a shift of focus to other alternatives, mostly radiation therapy as an alternative to surgery.[11,12] Overall, most of the initial studies showed higher perioperative mortality in pneumonectomy (5.9–6.2%) as compared to a lobectomy (1.5–3.2%).[13,14] The difference in perioperative mortality in pneumonectomy and lobectomy was not statistically different in our study (5% vs. 3.5%) and was similar to other recent studies that have reported a perioperative mortality rate of 1.8–5.3% after pneumonectomy.[9,15,16] The perioperative mortality in most series depend on the patient's age, the presence of comorbidities, use of induction therapy, surgical expertise, anesthesia care and postoperative management, and not just on the type of surgery performed.[17,18] Thus, similar perioperative outcomes with lobectomy and pneumonectomy in our study might be due to better patient selection, preoperative evaluation and optimization prior to surgery. Better patient selection is a key to success in any surgery and was possible with advances in the field of radiology and nuclear medicine, which helped to improve staging, assess resectability and further plan appropriate multimodality treatment plan. The preoperative cardiopulmonary clinical evaluation with lung ventilation perfusion scan (VQ) scan, diffusion capacity of lung for carbon monoxide (DLCO) and stress echo might have helped to identify patients optimally fit to undergo radical surgery. All patients had an intensive preoperative optimization with incentive spirometry, oral medications, and chest therapy with nebulization; which might have played a significant role in the optimal outcome.

In patients undergoing pneumonectomy, postoperative morbidity has been reported to be up to 59%, with atrial

Table 2: Comparison of patients in lobectomy versus pneumonectomy group

Variables	Pneumonectomy (n=20)	Lobectomy (n=28)	P
Mean age (years)	51.2	55.2	0.677
Sex (male/female)	15/5	23/5	0.282
Clinical presentation			
Symptomatic	19	20	
Incidental	0	4	
Surveillance	1	4	NS
Co-morbidities			
HTN	2	4	0.724
DM	1	2	1.000
CAD	0	1	0.282
Respiratory disorder	2	2	NS
ASA score (1/2/3/4)	0/10/7/3	1/11/12/4	NS
Clinical stage group			
Ia, Ib	0, 2	6, 3	
IIa, IIb	2, 5	2, 2	
IIIa, IIIb	7, 3	12, 0	
Metastatic	1	4	0.776
Neoadjuvant therapy	11	11	0.881

Staging according to AJCC 7th ed.ition, 2010. HTN=Hypertension; DM=Diabetes mellitus; CAD=Cardiac disease; AJCC=American Joint Committee on Cancer; ASA=American Society of Anesthesiologists

Table 3: Comparison of outcome after pneumonectomy versus lobectomy

Variables	Pneumonectomy (n=20)	Lobectomy (n=28)	P
Postoperative stay, mean (minimum-maximum±SD)			
ICU	4.45 (3-10±2.21) days	4.15 (3-7±1.19) days	0.620
Total	9.55 (6-18±3.18) days	10.32 (6-25±4.01) days	0.480
Blood transfusion	7	5	0.176
Arrhythmias	2	1	0.364
Prolonged air leak	1	3	0.480
Bleeding – re-exploration	0	0	-
BPF – pleural empyema	1	1	0.807
Perioperative death	1	1	0.807

SD=Standard deviation; ICU=Intensive Care Unit; BPF=Broncho-pleural fistula

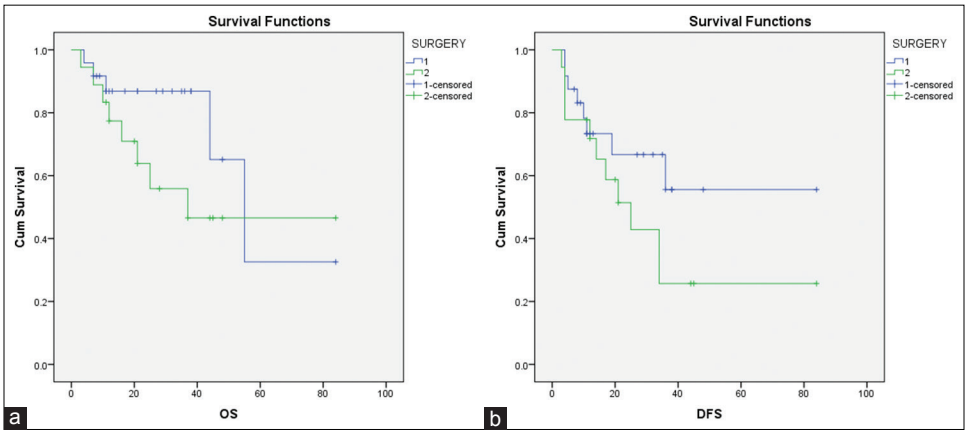

Figure 1: Comparison of overall survival and disease free survival in lobectomy (a) and pneumonectomy (b)

fibrillation being the most common complication.[1,7,18-21] Development of broncho-pleural fistula has been the most dreaded complication after pneumonectomy, the incidence has, however, come down due to the use of prophylactic autologous tissue transfer to cover the bronchial stump as has been seen in a study by Algar *et al*.[18] In our series, overall morbidity was similar in pneumonectomy and lobectomy (25% vs. 21.2%) with only one case of broncho-pleural fistula in each group, as a preemptive muscle flap was used in all patients at risk, especially patients undergoing pneumonectomy after induction therapy. ICU was also similar in the two groups in our study, reflecting comparable general condition, maintenance of vitals without any support and control of untoward event in early postoperative period. Similar hospital stay suggested similar recovery time as it relates to the time to implantable cardioverter-defibrillator D removal and return to basic activities.

With the advances in intraoperative monitoring and management, use of preemptive buttressing of the bronchial stump and aggressive postoperative care; pneumonectomy appears to be feasible and safe in selected cases to achieve optimal local control of disease and R0 resection. Right pneumonectomy was found to be more morbid in few studies, but we could not significantly differentiate right from left due to limited numbers in our series.[19] A constant decrease in the share of pneumonectomy in lung cancer management was also due to the concern regarding shorter long-term survival after pneumonectomy as compared to the parenchyma-preserving procedures.[14,22] In recent studies on the role of pneumonectomy for Stage III NSCLC, survival at 1, 3 and 5 years has been 66%, 38%, and 38%, respectively, which is far better than earlier reported series.[22,23] Similar to recent studies, improved overall and disease-free survivals were seen in pneumonectomy in our study, which were not significantly different from lobectomy group. Thus, this study supports the survival benefits seen in above-mentioned reports and favors pneumonectomy to remain in the list of surgeries for locally advanced lung cancers.

In Stage III lung cancer, multimodality treatment is preferred, as neo-adjuvant treatment may convert some unresectable tumors to resectable ones, without significantly affecting postoperative mortality, and this complete resection is seen to be essential for increasing survival.[24-31] In most studies, a survival benefit could not be appreciated in patients undergoing radical surgery after neoadjuvant therapy due to a higher rate of complications and mortality with pneumonectomy.[27,32] This held some patients to be offered the option of curative surgery. However, in recent few years many studies report the mortality rate for pneumonectomy to be significantly lower (as low as 6%) than that seen in intergroup 0139 trial (25%), which is acceptable and prevents these patients from being deprived of the survival benefit.[11,17,24,29,33-35] Other studies have focused on various other factors affecting the outcomes, like different chemotherapy regimens and response to them, methods of staging and restaging, and anatomical and cardiopulmonary factors assessed for selecting patients. These studies have further narrowed the difference in perioperative mortality solely based on type of surgery performed.[30,32,33,36] Stefani *et al*., performed pneumonectomy in 79 out of 175 (45.14%) patients operated after neoadjuvant therapy and reported that mediastinal downstaging was the best predictor of survival and better long-term survival with lower postoperative mortality could be achieved with radical surgery, including pneumonectomy.[37] In our series, more than half of the patients required neoadjuvant therapy and factors such as tumor size, central location, the presence of perihilar lymph nodes and posttherapy fibrosis compelled the requirement of pneumonectomy in 45.8% patients. Pneumonectomy was seen to be safe and feasible even after neoadjuvant therapy as there was no increase in perioperative mortality. In patients operated after neo-adjuvant therapy, similar median overall survival in patients undergoing pneumonectomy as compared to lobectomy, confirm the role of pneumonectomy in multimodality management.

A retrospective study with small numbers and short-term follow-up may be the lacunae in our study, but the results may open the gate for randomized trials re-evaluating the role of pneumonectomy for locally advanced cancers otherwise unfit for lobectomy, especially after neoadjuvant therapy.

Conclusion

Besides the type of surgery, surgical outcomes also depend on patient selection, careful optimization of medical conditions, response to neo-adjuvant therapy, perioperative

and postoperative monitoring and management. The present study shows that pneumonectomy may be safe, feasible and even beneficial in selected cases; if certain factors are considered during case selection. Pneumonectomy will, therefore, continue to play a role in the management of NSCLC in the present era.

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