Profile of Female Lung Cancer at a Tertiary Care Hospital in Kashmir Valley

Authors

Isha Puri¹, Fir Afroz², Nazir Ahmad Khan³, Shaqul Qamar⁴, Asifa Andleeb⁵, Paramjeet Puri⁶, Gul Mohammad Bhat⁷

¹Senior Resident, Radiation Oncology, Government Medical College Jammu
²³Professor Radiation Oncology, Skims
⁴Additional Professor Radiation Oncology, Skims
⁵Assistant Professor Radiation Oncology, Skims
⁶Assistant Professor, Dravyaguna, Government Ayurvedic Medical College Jammu.
⁷Professor Medical Oncology, Skims

Corresponding Author

Dr Isha Puri
Registrar Department of Radiation Oncology, Government Medical College Jammu,
Pin-180001 (J&K) India

Abstract

Purpose: To analyze the clinicopathological characteristics and the outcome of various treatment modalities used in management of lung cancer in females.

Methods: This was a retro-prospective study in which female patients with histological confirmed lung cancer who were registered at Regional Cancer Centre of Sher-i-Kashmir Institute of Medical Sciences, Srinagar between 2008 to 2014 were enrolled. Patient characteristics with regard to age, clinical presentation, locality, investigations, pathological characters and outcome of various treatment modalities were studied in detail. Data was compared using Pearson chi-square and Fischer’s exact test. P value <0.05 was considered to be statistically significant. SPSS version 20 was used for analyzing the data.

Results: A total of 298 patients were enrolled and 167 received treatment. Most patients were in the elderly age group (32.9%) and were from Srinagar district (29.9%). Dry cough was present in 71.4% of patients at presentation. Most common diagnostic modality used was bronchoscopy (58.05%). Squamous cell ca was most common histology (41.5%). Most (63.4%) patients were non smokers. 54.4% of patients had stage 4 at presentation. Chemotherapy alone was the most frequently used treatment modality (33.5%). Only 96 were available for response evaluation. During follow up, 3.12% had local failure and 27.08% had distant metastasis. Overall 1, 2, 3 and 6 year survival rates were 72.2%, 21.9%, 4.5% and 1.3% respectively. Triple modality treatment had highest survival rates followed by chemoradiation.

Conclusion: Delayed diagnosis and advanced disease were responsible for poor outcome. Early diagnosis and treatment and combined modality of treatment can improve survival.

Introduction

Lung cancer is one of the most common malignant neoplasm worldwide, accounting for more deaths than any other cancer cause.¹ The incidence is increasing globally at a rate of 0.5% peryear.² It remains the most lethal form of cancer in men and has now surpassed breast cancer in women as well in USA³. The worldwide incidence is 14% whereas it constitutes 6.8% of all cancers in India.⁴ In Kashmir it ranks second among all cases in males.
Although lung cancer has traditionally been thought of as a man’s disease, it is the second most common cancer and the leading cause of cancer deaths in women in the United States. The primary cause of lung cancer cases is smoking cigarettes. Women may have genetic and hormonal differences that affect the development of lung cancer in never-smokers as well as in those who smoke. Other risk factors include passive smoking. Non-small cell lung cancer accounts for nearly 85% and small cell lung cancer accounts for 15% to 20% of cases. Despite advances in imaging techniques and treatment modalities, the prognosis of lung cancer remains poor, with a five-year survival of 14% in early stages and less than 5% in locally advanced stages. Unfortunately only 20–30% of patients present with an operable disease, while most of the patients present in an advanced stage II and III. The main reason for late presentation in our country is the poor health awareness, delayed recognition and the poor referral of patients to the specialized centers. The present study was undertaken to analyze the demographic pattern, clinical presentation and pathological characteristics of lung cancer and to study the outcome of various treatment modalities used in the management of lung cancer at a tertiary care hospital in Kashmir, India.

Material and Method
All female patients with histopathologically confirmed lung cancer who were registered at Regional Cancer Centre of Sher-i-Kashmir Institute of Medical Sciences, Srinagar between 2008 to 2014 were enrolled in the study. This was a retro prospective study in which patient characteristics with regard to age, clinical presentation, locality, investigations, pathological characters, risk factors and outcome of various treatment modalities were studied in detail. Data was compared using Pearson chi-square test and Fischer’s exact test. P value <0.05 was considered to be statistically significant. SPSS version 20 was used for analyzing the data.

Results
A total of 468 female lung cancer patients were registered with regional cancer centre, SKIMS, Srinagar from 1st January 2008 to 31 December 2014. Out of 468 lung cancer patients only 298 were histopathologically confirmed.

Table 1- Age-Wise Distribution

| Age group (in years) | Frequency | %age |
|----------------------|-----------|------|
| <30                  | 22        | 7.4  |
| 30-40                | 2         | 0.7  |
| 40-50                | 46        | 15.4 |
| 50-60                | 70        | 23.5 |
| 60-70                | 98        | 32.9 |
| >70                  | 60        | 20.1 |
| Total                | 298       | 100  |

Most common age group was 60-70 years accounting for 32.9% of patients. Mean age for female lung cancer was 57.43 years.

Table 2- Clinical Presentation

| Symptoms               | NSCLC n=233 | SCLC n=65 | Total  |
|------------------------|-------------|-----------|--------|
|                        | N   | %    | N   | %    | N   | %    |
| Cough-dry              | 111 | 47.6 | 32  | 49.2 | 143 | 48.0 |
| Cough-Productive       | 61  | 26.2 | 9   | 13.8 | 70  | 23.5 |
| Hemoptysis             | 73  | 31.3 | 22  | 33.8 | 95  | 31.9 |
| Breathlessness         | 92  | 39.5 | 28  | 43.1 | 120 | 40.3 |
| Chest pain             | 58  | 24.9 | 12  | 18.5 | 70  | 23.5 |
| Hoarsness of voice     | 7   | 3.0  | 1   | 1.5  | 8   | 2.7  |
| Others                 | 57  | 24.4 | 11  | 16.9 | 68  | 22.8 |
| Asymptomatic           | 2   | 0.9  | 0   | 0.0  | 2   | 0.9  |

Most common symptom at presentation was cough 71.4% followed by breathlessness 40.3%, hemoptysis 31.9% and chest pain 23.5%.

Table 3-Histology

| Histology             | Frequency | %age |
|-----------------------|-----------|------|
| Squamous cell ca      | 123       | 41.5 |
| Adenocarcinoma        | 91        | 30.5 |
| Bronchoalveolar       | 13        | 4.4  |
| Small cell ca         | 65        | 21.8 |
| Large cell ca         | 5         | 1.7  |
| Adenoid cystic ca     | 1         | .3   |
| Total                 | 298       | 100  |

78.2% of the patients have Non-small cell lung cancer and 21.8% have Small cell lung cancer. Among NSCLC, squamous cell ca was most common (41.5%) followed by adenocarcinoma (30.5%), other histologies were only 6.4%.
Most [54.4\%] patients have stage 4 at presentation, followed by stage 3A [25.8\%], stage 3B [15.1\%], stage 2A [4.3\%], stage 1 [0.3\%].

Right upper lobe was the most common site in 23.2\% of patients followed by Right middle lobe in 18.8\%.

Out of 167 patients only 96 were available for evaluation of response. Response was evaluated by using Responsive Evaluation Criteria in Solid Tumors (RECIST) Criteria. Complete response was seen in 9.4\% of patients, partial response in 42.7\%, stable disease in 22.9\% and progression in 25\%.

Out of 298 patients, 56.04\% patients received treatment, 35.9\% did not receive and 8.05\% received palliative treatment. Chemotherapy was the most frequently used treatment modality in 33.5\% of the patients as most patients presented in stage 4. Radiation therapy in combination with chemotherapy, surgery and with both was delivered in 12.8\%, 0.34\% and 2.3\% of cases respectively.

Modality Overall 1, 2, 3 and 6 year survival rates were 72.2\%, 21.9\%, 4.5\% and 1.3\% respectively.
Discussion
Lung cancer is the most common fatal malignancy among men and women in most countries of the world and the gender difference is narrowing\(^9\). In India, the incidence of lung cancer is increasing rapidly, mainly due to progressive change in lifestyle. It remains a major health problem in the Kashmir valley and constitutes nearly 9.9% of all cancers.

Mean age for lung cancer in females was 57.43 years and it was comparable to males in study by Sheema Sheikh et al.\(^{10}\) The most common age group for female lung cancer was 60-70yrs [32.9%] which is contrary to 40-60yrs for males in study by Bhattacharyya Sujit Kumar et al\(^{11}\), Jagdish Rawat et al\(^{12}\).

Most of the patients were from Srinagar (29.9%) followed by Baramulla (14.8%), low prevalence was in districts- Bandipora (4.7%), Kulgam (3.4%), Kupwara (2.7%), Shopian (2.3%). These results were compatible with study by Parvaiz A Koul et al.\(^{13}\)

Most common symptom at presentation was cough 71.4% followed by breathlessness 40.3%, and it was comparable to study by Bhattacharyya Sujit Kumar et al.\(^{11}\). The duration of symptoms before diagnosis of cancer ranged from 3-6mths. More than 80% patients presented with multiple symptoms.

Out of 298 patients, 36.1% were smokers and 63.4% were non-smokers and smoking status was not known in 0.67% patients, it was comparable to study by Noronha V et al.\(^{14}\) Among smokers 42.9% smoked for 20-40 yrs, however duration was unknown in 52.3% of patients. 40% were hukka smokers, 10% both hukka and cigarettes smokers, type of smoking was unknown in 50% patients.

H/O Tuberculosis was present in 3.7% patients and COPD in 2.07%. These results slightly vary with the study by Sanjeet Kumar Mandal et al.\(^{15}\)

Xray chest and CT scan chest were done in all patients. Xray chest showed an abnormality in 95% of the cases. Most common modality used for confirming the histology was bronchoscopy in 58.05% patients followed by CT guided biopsy in 31.87% , and it was comparable to study by NA Khan et al.\(^{16}\)

Right sided lung cancer was more common [57.4%] than Left [42.6%] and it was comparable to study by Sanjeet Kumar Mandal et al.\(^{15}\)

Most of the patients had Non small cell lung cancer (78.2%), only 21.8% had Small cell lung cancer. Among NSCLC, squamous cell cancer was most common (41.5%) followed by adenocarcinoma (30.5%), which was comparable to study by Sheema Sheikh et al.\(^{10}\). Despite being more non smokers in our study, squamous cell ca was most common histology in females, this could be attributed to passive smoking. Among smokers 51.40% were sq cell ca, 26.17%-adenoca, 5.61%-brochoalveolar, 14.95%-small cell ca, 0.93% both large cell and adenoid cystic ca, which was comparable to study by Sheema Sheikh et al\(^{10}\) for sq cell ca.

Most of the patients had stage4[54.4%] at presentation, followed by stage3A[25.8%], stage3B[15.1%] which was comparable to study by Viswanath Sundaram et al.\(^{17}\) Bone was the most common site of metastasis in 25.3% followed by brain-17.3% and liver-14.8%. was in contrast to study by Noronha V et al.\(^{14}\) Lumbar spine is the most common site of bone metastasis followed by dorsal spine, femur, pelvis and ribs.

Out of 298 patients, 56.04% patients received treatment, 35.9% received no treatment, and 8% received palliative treatment.

Chemotherapy alone was the most frequently used treatment modality in 33.5% patients as most of the patients presented in stage 4. Other treatment modalities used were, Radiotherapy only-12(4.03%) patients, Surgery alone in 2(0.67%) patients, Radiotherapy + Chemotherapy- either concurrent or sequential- 38(12.8%) patients, Radiotherapy + Surgery - 1 (0.34%)patient, Chemotherapy + Surgery- Either adjuvant or neo-adjuvant-7(2.3%) patients, Radiotherapy + Chemotherapy + Surgery- 7 (2.3%) patients.

Of the 17 patients who had undergone surgery, lobectomy was done in 11 patients followed by pneumectomy, decortication and segmentectomy in 3,2 and 1 patients.
Of the 58 patients who received radiation, 14 received 60GY/30# and 44 received 45GY/20#.

Of the 152 patients who received chemotherapy, 100 patients received chemotherapy only, 37 patients received chemotherapy in combination with other modalities and 15 patients received Tyrosine kinase Inhibitors. Type of chemotherapy given depends on the histology. Various chemo combinations were: cisplatin and etoposide, paclitaxel and carboplatin, Gemcitabine and Cisplatin/Carboplatin, Pemetrexed and Carboplatin, cyclophosphamide and erlotinib. 37(27%) patients received <3 cycles, 45(32.8%) received 3-5 cycles and 55(40.1%) received 6 cycles.

Out of 167 patients only 96 were available for evaluation of response. Response was evaluated by using Responsive Evaluation Criteria in Solid Tumors (RECIST) Criteria. 9 patients (9.4%) had complete response, 41 patients (42.7%) had partial response and 22 patients (22.9%) had stable disease, 24 patients (25%) had progression of disease. Out of 9 patients who had complete response, 4 received triple modality i.e. radiotherapy + chemotherapy + surgery, 4 received radiotherapy + chemotherapy, 1 received chemotherapy + surgery.

During follow up, out of 96 patients, 3.12% had local failure and 27.08% had distant metastasis. Higher incidence of distant metastasis and local failure can be attributed to lower radiation dose[45Gy] and the fact that most of these patients did not complete the recommended schedule of chemotherapy.

Overall survival for CT+RT at 2.3 and 6yr was 13.5%, 10.8% and 2.7% and for CT+RT+SX at 2.3 and 6yr was 42.9%,14.2% and 14.2% and it was comparable to study by Shilpen Patel et al. Multimodality approach improves the overall survival compared to a single modality. Overall 1,2,3 and 6 year survival rates were 72.2%, 21.9%, 4.5% and 1.3% respectively.

Conclusion
The delayed diagnosis and consequent advanced disease are responsible for the poor outcome. A multi-modality approach to the treatment of lung cancer is advisable.

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