Risk Factor Profile of Lung Cancer Patients: A Study from the Himalayan State of Indian Subcontinent

Sharathbabu N Manjunath¹, Irappa V. Madabhavi², Malay S. Sarkar³, Satinder S. Kaushal⁴

¹Department of Cardiology, Jayadeva Institute of Cardiology, Mysore, Karnataka, India. ²Department of Medical Oncology, J. N. Medical College, Belagavi, Karnataka, India. ³Department of Pulmonary Medicine, Indira Gandhi Medical College, Shimla, Himachal Pradesh, India. ⁴Department of Internal Medicine, Indira Gandhi Medical College, Shimla, Himachal Pradesh, India.

Abstract

Background: Primary lung cancers in India were reported to be rare in earlier studies. But the trend is changing and there is increased incidence of lung cancers. Aims and Objectives: This present descriptive observational study was conducted to report the risk factor profile of the lung cancer patients from the Himalayan state of the Indian population. Materials and Methods: This descriptive epidemiological study was conducted from a single centre, in a prospective observational design, among the patients who were diagnosed as carcinoma lung histologically or cytologically over a period of one year in a tertiary care referral centre in the Himalayan state of the Northern India. The patients data was collected in detailed manner pertaining to age, sex, residence and occupation, questionnaires regarding risk factors like smoking history, Environmental tobacco smoke exposure, Indoor pollution, Alcohol history, HIV infection, Structural lung disease, Religion and Geography. Results: One hundred and one consecutive patients of primary lung cancer were recruited in the study which was confirmed either cytologically or histopathologically. Out of 101 patients, 79 (78.2%) were males and 22 (21.8%) were females, mean age was 62.65 years, 97 (96%) patients had rural background and 4 (4%) patients had urban background, 96 (95.04%) patients were active smokers, 3 (2.9%) were passive smokers and non smokers were 2 (1.9%), 25 (24.8%) were vegetarians and 76 (75.2%) were non vegetarians. 36 patients (35.6%) were from altitude of 0-1000 meters, 41 patients (40.6%) were from altitude of 1001-2000 meters, 21.8% were from altitude of 2001-3000 meters and 2% were from altitude of 3001-4000 meters. Adenocarcinoma was the most common type at all altitudes. Conclusions: Awareness about carcinoma lung in the Himalayan state especially in rural population is still lacking and are presenting at an advanced stage, which largely impact on survival of the patients. This study provides the data pertaining to risk factor profile of the lung cancer patients from the Himalayan state and can be utilised for future comparison with other Indian studies, to educate the community and to spread the awareness of the prevailing lung cancer risk factors.

Keywords: Lung cancer- Smoking- Himalayan state- Risk factors- Diagnosis

Introduction

Cancer of the lung was nearly nonexistent in the early 1900s. Previously in the 18th decade malignant tumors of the lung constitute only 1% of all cancers seen at autopsy, but due to progressive change in the lifestyle had risen to 10–15% by the early 1900s [1]. The term lung cancer is used for the tumors arising from the respiratory epithelium i.e. bronchi, bronchioles and alveoli. According to WHO classification, four major cell types i.e. squamous cell carcinoma (epidermoid cell carcinoma), small cell carcinoma, large cell carcinoma and adenocarcinoma including bronchoalveolar cell carcinoma makes up majority of all primary lung neoplasms [2]. Primary lung cancers in India were reported to be rare in earlier studies [3]. But the trend is changing and there is
increased incidence of lung cancers. Studies from India have emphasized the association of smoking habit and differences in relative risk rates in different communities based on smoking habit. Also occurrence of different histopathological types associated with different risk factors are studied in detail [4].

World Scenario

There is great variation in prevalence of lung cancer in different geographical areas. Nearly 70% of all new cases occur in developed countries. Among fatal malignant tumors, lung cancer and gastric cancer showed the highest frequency. There is definite increase in occurrence of lung cancer. The global risk among males is greater than 10-fold from less than 1% among the Indian population in Mumbai and Singapore to more than 14% in the Maori population of New Zealand. Estimates of the worldwide incidence and mortality from 27 cancers in 2008 have been prepared for 182 countries as part of the GLOBOCON series published by the International Agency for Research on Cancer. The most commonly diagnosed cancers worldwide are lung (1.61 million, 12.7% of the total), breast (1.38 million, 10.9%), and colorectal cancers (1.23 million, 9.7%). The most common causes of cancer deaths are lung cancer (1.38 million, 18.2% of the total), stomach cancer (738,000 deaths, 9.7%) and liver cancer (696,000 deaths, 9.2%) [5].

Indian Scenario

The national cancer registry programme of the Indian council of medical research collected data from six different parts of the country which showed varying figures in different areas including rural and urban areas [6]. This different data patterns have also been shown by multiple hospital data from different parts of the country. In patients of lung cancer, there is history of active tobacco smoking in 87% of males and in 85% of females. History of passive smoking is found only in 3% cases. In India, lung cancer is most common cancer in males in all urban registries. It is estimated that every year in India about 30,000 new lung cancer cases are registered. The ratio increases progressively up to 51 - 60 years and then remains the same. The smoker to non-smoker ratio is high up to 20:1 in various studies. The demographic pattern of lung cancer in India is similar to that of Western countries 40 years ago [7].

Many different type of risk factors are associated with lung cancer. Well known factors associated with lung cancer are smoking, [8, 9] environmental tobacco smoke exposure (ETS) and indoor pollution. Other factors associated are environmental exposure to arsenic and radon, [10, 11] petroleum exposure, alcohol consumption, hormone use, HIV infection, religion, geography, race etc. Evidence also exists regarding role of oncogenes and familial predisposition in lung cancer. Since early 1990s, mortality from lung cancer fell among men while it increased among women and is only now peaking among women, reflecting changing patterns of tobacco use over the past 30 years. Non-small-cell lung cancer constitutes 75 - 80% of lung cancers [12]. More than 70 % of them are in Stages III and IV, thus curative surgery cannot be done in these cases. The combined relative 5-year survival rate for all stages of lung cancer is currently 16%, slightly improved from 13% for lung cancers diagnosed in the 1970-80s [13].

Himachal Pradesh is a hilly area with diverse culture and practices and living habits. Majority of people are farmers and live in villages. Smoking habit is prevalent in both sexes, different age groups and in all forms. People use firewood for domestic purposes in ill ventilated environment because of lengthy winters. Also there are many other risk factors that have role in causation of lung cancer unexplored in this population. The purpose and novelty of our study is that we don’t have epidemiological data from the Himalayan states with respect to lung cancer and this study will definitely will focus on the risk factor profile of the different types of lung cancer patients from the Himalayan state and this data can be utilised for future comparison with other Indian studies, to educate the community and to spread the awareness of the prevailing lung cancer risk factors.

The aims and objectives of our study are, risk factors associated with carcinoma lung, and association between these factors with different histopathological types.

Materials and Methods

Patients and Study Design:

This single centre, descriptive observational, epidemiological study was a tertiary care hospital based study and was conducted in the department of medicine and pulmonary medicine, IGMC Shimla. This study was conducted among the patients who were diagnosed as carcinoma lung histologically or cytologically over a period of one year from July 1st 2011 to June 30th 2012, in a tertiary care referral centre in Northern India. The study was approved by the institutional ethical committee and review board [IEC-IGMC SHIMLA-M6/2011]. Prior consent was taken from all the patients for inclusion in this prospective observational study.

Inclusion Criteria

All indoor patients and referred patients who have been proved of having carcinoma lung either in histopathology or cytology on or after May 1st, 2011 were selected as study patients.

Exclusion Criteria

Patients suspected to be carcinoma lung by any other way other than cytology or histopathology are excluded from our study. The cases proven by any method before May 1st, 2011 are excluded.

The patients included in the study were subjected to detailed work up including name, age, sex, and residence. Questionnaire regarding risk factors was included in detailed history which includes: Basic detail as above, smoking history in detail, Environmental tobacco smoke exposure, Indoor pollution, Alcohol history, HIV infection, Structural lung disease, Religion, Geography and the clinical history regarding type of lung cancer has taken
WHO classification for primary lung tumors was used to classify the lung cancer into different histopathological types: Squamous cell carcinoma, Small cell carcinoma, Adenocarcinoma, Large cell carcinoma. When the cell differentiation was not clear, the tumor was termed as ‘undifferentiated carcinoma’ [2].

The confirmed cases taken for study are classified as those proven on cytology and histopathology. The data thus collected was analysed and all the patients were compared with each other regarding age, sex, place of residence, type and duration of symptoms, detailed smoking history, presence or absence of metastasis and other risk factors. The findings of this study were compared with similar studies done earlier in this part of the country.

Statistical Analysis
Data collected was managed on a Microsoft excel spreadsheet. Categorical & continuous variables of the clinical characteristics of study population was described as percentages & Means±SD respectively & Chi-Square test was used to compare significance of difference in the distribution of discrete variables. Non-parametric test Mann-Whitney test was used to compare the significance of difference in means of continuous variables. 2 tailed significance at <0.05 was used as statistically significant. All analysis was performed with the Epi-Info version 3.5.1.

Results

Sex distribution
Out of 101 patients included in the study, 79 (78.2%) were males and 22 (21.8%) were females. The male female ratio was 3.59:1. Among the histopathological types, adenocarcinoma was the leading type in both males and females constituting around 36.6% of the total cases (Table 1).

Age distribution
The age group of study population ranged from 33 years to 86 years. The mean age of lung cancer in this study was 62.65 years with Standard Deviation of 9.5356. Majority of the patients [14] were in age group 61-70 years (38.6%) (Table 2).

Rural/Urban background
Ninety seven patients (96%) out of 101 patients had rural background and only 4 (4%) patients had urban background (Table 2).

Table 1. Showing Different Histopathological Types in the Study Group

| Histopathological Types           | Male-79 (%) | Female-22 (%) |
|----------------------------------|-------------|---------------|
| Squamous cell carcinoma          | 21 (87.5)   | 3 (12.5)      |
| Small cell carcinoma             | 16 (80)     | 4 (20)        |
| Adenocarcinoma                   | 25 (67.6)   | 12 (32.4)     |
| Large cell carcinoma             | 4 (80)      | 1 (20)        |

Altitude
Patients included in the study were distributed according to altitude of living places. 36 patients (35.6%) were from altitude of 0-1000 meters, 41 patients (40.6%) were from altitude of 1001-2000 meters, 22 patients (21.8%) were from altitude of 2001-3000 meters and 2 patients (2%) were from altitude of 3001-4000 meters. Adenocarcinoma was the most common type at all altitudes constituting around 37 (36.6%) of the total cases. But among histopathological types, squamous cell carcinoma 11 (45.8%) and large cell carcinoma 3 (60%) types were common at altitude less than 1000 meters and rest were common at altitude 1001-2000 meters (Table 3).

Smoking
Majority of our study population was active smokers with total of 96 (95.04%) patients. Among different histopathological types, all were common among active smoker group. Among total 99 smokers, 83 (83.83%) were active smokers, 13 (13.13%) were both active and passive smokers and 3 (3%) were passive smokers. In relation to type of lung cancer, adenocarcinoma was the most common among all kind of smokers [15] and non smokers (4) except among cigarette smoking group, bidi-cigarette group and bidi-hookah group where squamous cell carcinoma (4), small cell (2) and squamous cell (4) type of carcinomas were common (Table 4 and Table 5).

Biomass fuel exposure
All the individuals taken in the study had exposure to biomass fuel. Hence it can be concluded that this factor had definite relation with incidence of lung cancer. Adenocarcinoma was seen in 37 patients and was the most common type associated with biomass fuel exposure.

Environmental smoke exposure
Among 101 candidates selected for the study, only 8 (7.9%) patients had significant environmental smoke exposure. Among non-exposed, adenocarcinoma [16] was the commonest type and in the exposed (small cell carcinoma [17], adenocarcinoma [17] and undifferentiated type [17] were equally common).

Alcoholism
Among total 101 patients, 58(57.4%) were non alcoholics and 43 (42.6%) were alcoholics. It had significance in incidence of specific type of lung cancer. Among non-alcoholics, adenocarcinoma-25 (67.6%) was the most common type but in alcoholics, squamous cell carcinoma-14 (58.3%) was the most common type.

Post tubercular state
Among 101 candidates, only 7 (6.9%) patients had history of tuberculosis. Post tubercular state had no much significance on type of lung cancer since adenocarcinoma was the most common type in both (33 and 4) groups.

Diet
Among the study candidates, 25 (24.8%) were
vegetarians and 76 (75.2%) were non vegetarians. Thus, from our study it can be concluded that red meat had significant correlation with incidence of lung cancer. Adenocarcinoma was the most common among both groups indicating no much influence of diet on incidence of specific type of lung cancer. Among histopathological types, all types were common in nonvegetarians except undifferentiated type which was common in vegetarians. (Table 2).

Other factors
The other factors correlated with incidence of lung cancer in our study did not have much influence. All candidates in our study were HIV non-reactive (100%); none of the candidates had neither family history of lung cancer nor any structural lung disease (100%). All the candidates were from Hindu religion (100%).

Discussion (Table 6)
In India, lung cancer is among the leading causes of cancer with male to female ratio ranging from 2.9 to 7.8 [18-20]. In our study, 79 (78.2%) were males and 22 (21.8%) were females. The male female ratio was 3.59:1. This finding was also consistent with study from our institution 10 years before which showed 83.97% males and 16.03% females with male female ratio of 5.23 [4, 12]. Our findings were also comparable to Indian studies as well as to studies from other countries [3, 12, 21-23]. During 1985-1995, as a result of changes in tobacco consumption, the incidence rates increased by 56% in men and by 5% in men under the age of 65. Still male dominance continues among lung cancer cases. With respect to histopathological type, all types were common in females [22].

Himachal Pradesh is a hilly state with majority of population forming part of rural areas. The same scenario reflected in our study with ninety seven patients (96%) out of 101 patients from rural background and only 4 (4%) patients from urban background. In the study from our institution 10 years before also showed majority population from rural background (97.2%) [3]. This was also consistent with other Indian studies which showed around 80% of lung cancer patients from rural areas. Within different histopathological types, major part was from rural background among all types [3, 21-23].

Lung cancer tends to occur in 5th to 6th decade and average age of presentation in Indian patients is found to be 46.6-57.7 years by different studies [18-20, 24-25]. Jindal and Behera have reported the largest series of 1009 lung cancer cases and mean age of presentation was 54 years. In our study the mean age of presentation was 62.65 years. Also, this is consistent with study from our institution 10 years before which showed mean age of 60.16 years. Majority of population in our study (38.6%) were between 61- 70 years of age. This was different from study from our institution 10 years before which showed most cases (36.79%) in age group of 51-60 years.
The peak age of patients of lung cancer has shifted from 6th to 7th decade. The mean age of presentation in our study is slightly early as compared to studies from other countries where it ranged from 68-75 years [17,26].

Smoking is the most common causative factor in lung cancer. All types and all forms are known to be associated with incidence of lung cancer. Smoking in all forms is prevalent in this part of the country in both sexes and in both rural and urban areas. Majority of population in our study were smokers (94.95%) and the smoker non-smoker ratio was 19.2. This was consistent with study from our institution 10 years before which showed 94.3% of smokers with smoker non-smoker ratio of 11.5-19 [26, 28]. Our findings were much higher as compared to other studies from India (2.7-7.3) [18-19, 24, 27]. But these findings were consistent with studies from other countries where smoker non-smoker ratio ranged from 11.5-19 [26,28].

Passive smoking is also a significant risk factor in lung cancer. In our study among total 99 smokers, 13 (13.13%) were both active and passive smokers and 3 (3%) were passive smokers. There is also evidence that nonsmoker females married to smokers are at risk for lung cancer. A meta-analysis of 41 studies showed that environmental tobacco exposure carries a relative risk of development of lung cancer in both males and females. Reynolds summarized the evidence on workplace exposure to secondhand smoke and lung cancer risk [29]. In the study by Buffett et al. [30] it was reported that the association between workplace ETS and squamous cell carcinoma was stronger than for either adenocarcinoma or small cell carcinoma. A study by Wapiti et al has shown that environmental tobacco smoke exposure during childhood is strongly associated with the risk of later development of lung cancer.

In our study, the commonest type of lung cancer is adenocarcinoma (36.6%). In study done 10 years back at our institution, it was squamous cell carcinoma (46.2%) that was the most common type of lung cancer and was consistent with increased smoker non-smoker ratio. There were studies suggesting increasing trend in incidence of adenocarcinoma. A study by P.N. Chhajed et al [31] had also reported increased incidence of adenocarcinoma in their study. Adenocarcinoma of the lung, once considered minimally related to cigarette smoking, has become the most common type of lung cancer in the United States. The increased incidence of this cancer might be explained by advances in diagnostic technology. There is also evidence that changes in cigarette design (e.g., the adoption of filter tips), or changes in smoking practices might be a reason for this change. Despite widely variable figures from Indian literature, undifferentiated carcinoma appears to be less frequent in India and ranged from 4.2 to 21%. Similar findings were noticed in our study (13.9%) in contrast to much lower incidence (4.7%) as seen in study from our institution 10 years back.

In Himachal Pradesh, most of the cases are from rural population and majority smoking is in the form of bidis. Other forms in the form of cigarette, hookah and combination are also seen. In our study 77 (80.2%) were bidi smokers, 6 (6.25%) were cigarette smokers, 4 (4.1%) were bidi and cigarette smokers, 4 (4.16%) were bidi and hookah smokers, 4 (4.1%) were all bidi, cigarette and hookah smokers, 1 (1%) was other form of smoker. In the study 10 years before at our institution, majority were bidi smokers (95%) and hookah smokers (20.8%). Cigarette smokers were (12.8%). Overall if we analyze, there has decrease in bidi and hukka smokers and relative increase in cigarette smoking which supports increase incidence of adenocarcinoma in our study. This correlation has been supported by Michael J. Thun et al. [32].

Most of our patients had smoking index of 0-500 (65.6%), 27 (28.1%) had index of 501-1000 and 6 (6.2%) had an index of 1001-1500. This was similar to the finding observed in the study conducted 10 years back in this region [25]. All types of lung cancer were common at lower smoking index.

Biomass fuel exposure is an important risk factor in lung cancer. In our study all had significant exposure to
biomass fuel. Behera et al [33] also showed that biomass fuel exposure is a significant risk factor in lung cancer. In their study female population was taken as they had majority of nonsmokers and mainly biomass fuel exposure was studied as a risk factor. Majority of our study population was from rural background and use unprocessed solid fuel for cooking. Himachal Pradesh is also having cold climate during most of the time in a year and people use biomass fuel for heating purpose also. The effect of coal fumes from heating or cooking in poorly ventilated houses on lung cancer has drawn attention. A study from China showed a good correlation between indoor air pollution as measured by benzopyrene concentration and high lung cancer mortality rates. In one of the Indian retrospective analysis study by Gupta et al [15] on risk factors of lung cancer, cumulative exposure of >45 years in women to indoor population from use of coal or wood for cooking or heating showed noteworthy results.

Environmental smoke exposure is one of the important risk factors in lung cancer. In our study, out of 101 patients only 8 (7.9%) patients had significant environmental smoke exposure. Among nonexposed, adenocarcinoma was the commonest type. Among exposed, small cell carcinoma, adenocarcinoma and undifferentiated type were equally common. The decreased count in our study might be due to the reason that majority of our study population is from rural background. Urban air contains many known carcinogens and exposure to this has shown to predispose to lung cancer in UK and US.

Alcohol consumption has also much influence on incidence of lung cancer. In our study 58 (57.4%) were non alcoholics and 43 (42.6%) were alcoholics. In our study population majority were from rural background and type of drink was local made in significant amount. Among nonalcoholic’s, adenocarcinoma was the most common type but in alcoholics, squamous cell carcinoma was the most common type. Eva Prescott et al [34] conducted study on influence of type of alcoholic beverage on lung cancer incidence and concluded that in men, a high consumption of beer and spirits is associated with an increased risk of lung cancer, whereas wine intake may protect against the development of lung cancer. Several case-control studies have reported an increased risk of lung cancer with alcohol intake, although others have found no association. Jo L Freudenheim et al [35] in their pooled analysis of cohort studies concluded that a slightly greater risk of lung cancer was associated with the consumption of ≥30 g alcohol/day than with no alcohol consumption and alcohol consumption was strongly associated with greater risk in male never smokers. According to Mayo Clinic data, drinking more than a moderate amount of alcohol- no more than one drink a day for women or two drinks a day for men may increase risk of lung cancer.

Post tubercular state is also a risk factor in lung cancer. [16]. In our study out of 101 patients, only 7 (6.9%) had history of tuberculosis. Wu CY et al [36] conducted a population-based cohort study and concluded that pulmonary infection with tuberculosis is associated with an increased risk of lung cancer.

HIV status, structural lung disease and religion have been mentioned as risk factors in lung cancer. But in our study all patients were negative for HIV, all were from

### Table 6. Showing Comparison of the Present Study Findings with the Study Done in this Area 10 Years Back

| Parameters                  | 2002 Study [32] (%) | Present 2012 study (%) |
|-----------------------------|---------------------|------------------------|
| Sex                         |                     |                        |
| Male                        | 83.97               | 78.20                  |
| Female                      | 16.03               | 21.80                  |
| Background                  |                     |                        |
| Rural                       | 97.20               | 96                     |
| Urban                       | 2.80                | 4                      |
| Age group                   |                     |                        |
| Most common                 | 51-60 years         | 61-70 years            |
| Percentage                  | 36.8                | 38.6                   |
| Smoking                     |                     |                        |
| Smokers                     | 133 (94.3)          | 94.95                  |
| Smoker: non smoker          | 30 (20.2)           | 19.2                   |
| Form of smoking             |                     |                        |
| Bidi                        | 133 (95)            | 92.30                  |
| Hookah                      | 31 (20.8)           | 8.20                   |
| Cigarette                   | 20 (12.8)           | 14.45                  |
| Histopathological type      |                     |                        |
| Squamous cell carcinoma     | 69 (46.2)           | 19.80                  |
| Small cell carcinoma        | 45 (23.5)           | 23.70                  |
| Adenocarcinoma              | 20 (13.2)           | 36.60                  |
| Large cell carcinoma        | 14 (9.4)            | 4.90                   |
| Undifferentiated & mixed    | 10 (6.5)            | 14.80                  |
Hindu religion.

Dietary factors have a significant role in lung cancer incidence. In our study 25 (24.8%) were vegetarians and 76 (75.2%) were non vegetarians. Case control studies from China have shown that vegetable intake is a protective factor for lung cancer. Dietary cholesterol and animal fat increase the risk of lung cancer. Ganesh et al [14] conducted a case control study of risk factors for lung cancer at Mumbai where it was concluded that among dietary items only red meat consumption showed a 2.2-fold significant excess risk of lung cancer. In our study, majority were non vegetarians consuming red meat. Alavanja et al also showed consumption of red meat to be associated with lung cancer. Eduardo et al showed that adenocarcinoma was positively associated with fried, barbecued and salted meat [37].

Family history also has some role in lung cancer. Our study did not have any patients with family history of lung cancer. Susan et al supported the hypothesis of a genetic susceptibility for lung cancer [38]. Mayo clinic data showed people with a parent, sibling or child with lung cancer have an increased risk of the disease [39].

Future Implications

Based on the findings of this study we suggest that smoking awareness programmes must be strongly promoted by the Government and the laws prohibiting smoking in public places should be strictly implemented. The teaching about ill effects of smoking must be a part of education programme at school level. The role of modification of risk factors other than smoking should not be neglected. Studies implicating the role of risk factors other than smoking are required in future.

In conclusions, lung cancer is a major health problem in India and also worldwide. There are many variations in the epidemiology of lung cancer in last few decades. In this tertiary care hospital-based study from the Himalayan region we studied the risk factor profile in 101 consecutive lung cancer patients. In comparison of our study with the study conducted 10 years back in this region, there are changes with respect to risk factors and the incidence of histopathological type of lung cancer. In our study, the most common histopathological type is adenocarcinoma in contrast to squamous cell carcinoma which was the most prevalent type 10 years back. Lung cancer is still more common among males and majority of the population is from rural areas which is similar to that of previous study. The common age group of incidences of lung cancer has shifted from 6th decade to 7th decade. Bidi smoking is still the most common form of smoking but cigarette smoking population is increasing which has relevance in the increasing incidence of adenocarcinoma. All of the study population had biomass fuel exposure. Only 7.9% of the population had environmental smoke exposure. The limitation of our study was that control group was not taken.

Limitations of the Duty

As this is a prospective single centre, short period observational study with small number of patients. We should conduct long term, multi centric prospective randomised controlled studies to understand the cause and effect relationship on the patients.

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None.

Conflicts of Interest

None.

Ethical Statement

No ethical issues while publishing this article.

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