

# Female lung cancer in Marrakech

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## ABSTRACT

**Background:** To evaluate the epidemiological aspect of lung cancer in women in Marrakech city in Morocco. **Methods:** This is a retrospective study conducted between 2003 and 2009 in the Department of Oncology-Radiotherapy, University Hospital Mohamed VI Marrakech. **Results:** Twenty nine women with lung cancer were unrolled (9% of all lung cancer). The average age was  $55.7 \pm 12$  years. Only twenty percent of our patients were smokers while 38% reported a greater or lesser exposure to passive smoking. Ninety percent of patients were housewives and 62% were from rural areas and all reported massive exposure to smoke from cooking fuels which was mainly charcoal. Squamous cell carcinoma represents 67% of cases. Tumors were diagnosed at advanced stages II/IV in 81% of cases. Eight patients received neo-adjuvant chemotherapy followed by radio-chemotherapy combination and palliative chemotherapy has been indicated in twelve patients. Nine patients received best supportive care. Average follow-up was of twelve months. Fourteen patients were lost to follow-up. Among fifteen evaluable patients, response was noted in seven patients, stabilization in four patients and progression in four patients. **Conclusion:** Female lung cancer is a relatively rare condition in Marrakech, Morocco. Although the role of smoking in the pathogenesis of lung cancer is clearly established; there are other risk factors including hormones that make women more susceptible to carcinogens of tobacco. Other geographical and environmental factors could be incriminated including domestic smoke exposure especially in our context.

**Key words:** Adenocarcinoma, female, lung cancer, squamous cell carcinoma

## INTRODUCTION

Lung cancer is one of the leading causes of mortality in the world in both developed and developing countries. It is the most widespread carcinoma with a poor prognosis. Currently, men are the most affected, but in recent years there has been a rapid increase in lung cancer mortality among women in both industrialized and developing countries. The literature shows clearly that lung cancer in women differs from that in men in several specific aspects. Actually, the role of smoking is being clearly established in the onset of the lung cancer in women in industrialized countries. Various epidemiological studies have demonstrated the role of other factors acting either

as independent risk factors or interacting with the effect of smoking. In addition, only 70% of women with lung cancer is smoker and female smokers who develop lung cancer smoked lesser in duration and in quantity than their male counterparts. However, outcomes seem to be different: In fact, women have better survival than men regardless of stage, histology or therapy. Furthermore the role of environmental factors and lifestyle can change from one geographic area to another and according to socioeconomic factors. In addition there is a controversy regarding the thesis stating that the women have a susceptibility to tobacco carcinogens that may be greater than men. Consequently, female lung cancer is a separate entity that requires several studies to define its epidemiological, clinical and therapeutic characteristics.

## PATIENTS AND METHODS

This is a retrospective study conducted between 2003 and 2009 in the Department of Oncology-Radiotherapy, University Hospital Mohamed VI Marrakech. We included only women with histologically proven lung cancer in our study.

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## RESULTS

We had identified 325 patients with lung cancer during this period, only 29 were female (9%). Table 1 summarized the epidemiological, clinical and histological characteristics of women with lung cancer in our institution. The average age was  $55.7 \pm 12$  years. Twenty percent of our patients were smokers while 38% reported a greater or lesser exposure to passive smoking. Ninety percent of patients were housewives and 62% were from rural areas and all reported massive exposure to smoke from cooking fuels which was mainly charcoal. Regarding pathology, it was a squamous cell carcinoma in 67% of cases, adenocarcinoma in 24% and small cell lung cancer in 9% of cases. Dyspnea was the major clinical sign found in 72% of patients, hemoptysis was reported in only 55% of our patients. Thoracic CT scan was used to cancer staging; tumors were diagnosed at stage IV in 52% of cases, at stage III in 29%, at stage II in 19%. Eight patients received neo-adjuvant chemotherapy followed by radio-chemotherapy combination, and none of our patient could receive surgery. Palliative chemotherapy has been indicated in twelve patients. Nine patients received best supportive care. Average follow-up was of twelve months. Fourteen patients were lost to follow-up. Among fifteen evaluable patients, response was noted in seven patients, stabilization in four patients and progression in four patients.

## DISCUSSION

The incidence of lung cancer in females in our country remains low compared to the industrialized countries. In fact, the standardized incidence of female lung cancer in Moroccan patients is 2.9 compared to 12.6 in France<sup>[1]</sup> and 52.3 in USA.<sup>[2]</sup> Several studies, from mostly the North American, report the hypothesis that women may have a heightened sensitivity to carcinogens in tobacco. In addition, the risk of developing lung cancer in smoker women is 1.5 to 3 times higher than that of men with equal smoking.<sup>[3,4]</sup> Other

European studies have not found significant difference between men and women in the occurrence of lung cancer with equal smoking.<sup>[5]</sup> Passive smoking is the most studied risk factor of lung cancer in the literature. Relative risk differs depending on the type of exposure: Family, professional or social,<sup>[6]</sup> the intensity of tobacco smoking of responsible person<sup>[7]</sup> and the continued or interrupted character of the exposure.<sup>[8]</sup> In addition, several studies have tried to clarify the role of hormones in the occurrence of lung cancer in women. It seems well established that estrogens are able to induce chromosomal alterations and genetic mutations that can lead to adenocarcinoma.<sup>[9]</sup> In fact, estrogens may act as a tumor promoter through a mechanism mediated by receptors. They are also implicated as a direct carcinogen after activation to catechol estrogens which can form adducts with DNA.<sup>[10]</sup> Although professional exposures are less common in women, a study demonstrated a higher incidence of lung cancer among women in the profession at risk; such as the bus drivers and tramway.<sup>[11]</sup> The role of the home environment is important in case of the present study population which mostly comprised of housewives from rural areas. Exposure to smoke from fuel used for cooking or heating is frequent. On the other hand, the consumption of green vegetables in large quantities and fruits rich in vitamin C is found as a protective factor of lung cancer<sup>[12,13]</sup> with relative risks to a control population between 0.4<sup>[12]</sup> and 0.79.<sup>[13]</sup> Data on the age at diagnosis in the literature are discordant. Perrot, *et al.*,<sup>[14]</sup> reported a mean age at diagnosis of 61 years in 198 women and  $62 \pm 10$  years in 839 men managed with surgery for non-small cell lung carcinoma. However, two North American studies<sup>[15,16]</sup> reported a significantly lower age at diagnosis among women. In our series, the mean age was lower among women 55.7 years vs 59.5 years among men. Clinically, several studies have compared the presented symptoms at diagnosis. Perrot *et al.*,<sup>[14]</sup> pointed out that 32% of women versus 20% of men were non-symptomatic at diagnosis. Moreover, when they were symptomatic, patients presented less hemoptysis, less pleuropulmonary infections, less chest pain and lower frequency of weight loss. An American study<sup>[17]</sup> showed a higher frequency of digital clubbing in women (40% versus 19% in men). Coughing is also more common in women with lung cancer (15% versus 11% for men).<sup>[17]</sup> About the evolution of weight, women lose less weight compared to men during the period of treatment.<sup>[18]</sup> Our results are in concordance with those of literature; the predominant clinical sign was dyspnea. Hemoptysis was less frequent; however none of our patient had digital clubbing. In addition, a Polish study<sup>[19]</sup> showed that women had more frequently a metastatic disease at diagnosis (20.3% versus 13.9% in men). Several studies have reported that the predominant histological form of lung cancer in female was adenocarcinoma, especially in non-smoking young women.<sup>[20-22]</sup> Smoking whether active or passive

**Table 1: Summary of the epidemiological, clinical and histological characteristics of patients**

Number of patients	29 women among 325 patients
Average age	55.7 years
% Smokers	21
% Exposure to passive smoking	38
% Exposure to smoke from cooking fuels	93
% main symptoms	Dyspnea 72 Hemoptysis 55
Pathology %	Squamous cell carcinoma 67 Adenocarcinoma 24 Small cell lung cancer 9
Stages %	Stage VI 52 Stage III 29 Stage II 19

is more implicated in the occurrence of squamous cell carcinoma.<sup>[23-26]</sup> In a meta-analysis,<sup>[27]</sup> adenocarcinoma occurs more frequently among non-smoking women than women exposed to tobacco.

In this study, we found that squamous cell carcinoma was more frequent than adenocarcinoma, this can be explained by the higher percentage of exposition to passive smoking. The inclusion of women in clinical trials investigating the management of lung cancer was extremely low. Recent studies have shown that women were more often operated for lung cancer than men (23.2% vs. 18.8% men).<sup>[10,17,28]</sup> Men underwent more pneumectomy while women more segmentectomy.<sup>[17]</sup> This could be explained by the peripheral nature of lung adenocarcinoma more common among women. In our series no patient had a surgery probably due to the advanced stage of disease at diagnosis, which is a consequence of the difficulty of access to care in our context. About the response to treatment, no data in the literature shows significant difference in efficacy of chemotherapy between men and women.<sup>[9]</sup> However, for gefitinib, the female gender appears to be an important predictor of response.<sup>[29,30]</sup> The National Cancer Institute of Canada Clinical Trials Groups (NCIC CTG) compared in a clinical trial (BR 21) erlotinib with placebo after failure of standard chemotherapy of non-small cells lung cancer. In this study, there was a higher overall response rate among women (14.4% vs. 6% in men). It seems that women are more susceptible to chemotherapy complications. Indeed, hospitalization time, whatever the issue, tends to be significantly longer in women.<sup>[31]</sup> In the series of Cancer and Leukemia Group B (CALGB), involving 1479 patients with a small cell lung cancer, in different trials the female appears to be a predictor of severe hematological toxicity.<sup>[32]</sup> About complications of radiotherapy, Robnett *et al.*,<sup>[33]</sup> showed that women are more likely to develop severe radiogenic pneumonia than men in a multivariate analysis. Several recent series found better overall survival in women, all histological types combined. A Japanese study<sup>[34]</sup> compared 131 women and 361 men operated for lung cancer, there was better survival among women in particularly because of the higher incidence of adenocarcinoma in women known more operable.

## CONCLUSIONS

Although the role of smoking in the pathogenesis of lung cancer is clearly established; there are other risk factors including hormones that make women more susceptible to carcinogens of tobacco. Other geographical and environmental factors could be incriminated including domestic smoke exposure especially in our context. This inter-sex variability exceeds susceptibility to risk factors and affects the clinical, pathological and therapeutic aspects of lung cancer. This is a

rational to conduct studies on a larger scale.

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