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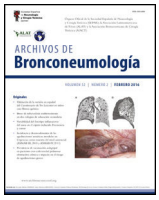

Editorial

Lung Cancer Unrelated to Smoking☆

Cáncer de pulmón no relacionado con el tabaco

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Lung cancer (LC) is the most common cancer worldwide in men and the third most common in women, and the first cause of cancer death in both sexes in developed countries.[1] Smoking is clearly the most significant carcinogenic factor, but in recent years LC in never-smokers has become a growing public health problem: viewed as an independent entity, LC unrelated to smoking constitutes the seventh cause of cancer worldwide, ahead of tumors such as pancreatic or prostate cancers.[2] Around 25% of all cases of LC worldwide occur in never-smokers, and recent studies suggest that this incidence is growing.[3]

Robust epidemiological evidence indicates that the main risk factor for LC in never-smokers is exposure to residential radon.[4,5] The second greatest risk factor in terms of strength of association is the individual's occupation. Occupational carcinogens, such as asbestos, cadmium, and arsenic, increase the risk of LC, and some workers, such as stone masons, construction workers, painters, joiners, carpenters, mechanics, shipyard workers, are at greater risk. Since the introduction of anti-smoking legislation, workers in the hospitality sector are no longer included in the high-risk group. The risk of LC in never-smokers also appears to be higher[6] in individuals who practice certain leisure activities, such as DIY or painting, and in those exposed to environmental pollution[7] and indoor pollution from burning biomass or oil in open-fire stoves, particularly in homes without proper ventilation. Finally, it has been clear for some time now that exposure to environmental tobacco smoke (ETS) also increases the risk of LC. It is worth noting that although the risk of LC attributable to ETS exposure is around 1.3, this type of exposure is widespread, and can lie behind a significant number of cases. Genetic susceptibility also plays a part in the development of LC, although this is less important than for other cancers, since penetrance is low. LC risk factors in never-smokers thus can be classified as modifiable (extrinsic) or non-modifiable (intrinsic).[8]

As LC has conventionally been associated with smoking, scant evidence has been generated on risk factors in never-smokers.

The results of some studies have led to the theory that LC in never-smokers is a different disease from LC in smokers and ex-smokers, with different carcinogenic mechanisms, molecular alterations, clinical characteristics, and even different prognoses.[3] The most important of these differences, due to their implications in treatment and disease prognosis, are those which affect the gene driver mutation profile. EGFR mutations, for example, occur far more frequently in never-smokers than in smokers and former smokers, and constitute a prognostic and predictive variable for response to treatment with tyrosine-kinase inhibitors,[9] routinely tested in stage IV adenocarcinoma.

The study of risk factors for LCs not associated with smoking is complex, primarily due to the low incidence of the disease in never-smokers. Some risk factors, such as occupation, are difficult to quantify: an individual may have had several jobs during their working life, some with and some without exposure to carcinogens, and in case of exposure, with highly variable intensity. The characterization of environmental pollution, or even passive smoking, is similarly difficult. However, one of the main risk factors, exposure to residential radon, is relatively simple to measure by installing a radon detector in the patient's home. Radon maps are also of great epidemiological value, particularly in geographic areas of high exposure, such as Galicia or other areas of Spain. The Galician Radon Map is a project run by the Galician Radon Laboratory that currently has readings from more than 3400 homes in this autonomous community.[10] These maps are a useful tool for identifying geographic areas with a high concentration of indoor radon, and could be used to intensify prevention measures in these high-risk areas. Indeed, if a never-smoker develops LC, possible exposure to radon in the home must be investigated. In countries such as the United States, United Kingdom and Ireland, radon maps are available to the public. In Spain, no effective prevention policies against exposure to residential radon have yet been implemented; however, a European directive published in January 2014, regulating exposure to radon in the home, specifies that domestic concentration must not

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exceed 300 Bq/m^3. The same limit applies to the workplace. This directive, which should be incorporated into national law in February 2018, urges member states to develop action plans to address the risks arising from exposure to residential radon. Its implementation offers a historic opportunity to educate the general public and health authorities to raise awareness of the effects of exposure to residential radon on health in Spain. We were able to implement anti-smoking policies (which must remain in place until the final goal of eradicating smoking in our society is achieved), and now we must address the problem of exposure to residential radon. This will only be possible when the public authorities become fully committed to reducing exposure of the population to this carcinogen and to raising awareness of the risks associated with exposure to indoor radon.

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