

Ablating lung cancer, knowing the tumor better

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Globally, lung cancer is the most common cause of cancer death. Lung cancer incidence and mortality have a direct relationship with tobacco smoking addiction, that is increasing in regions with lower human development index, such as Asia and western Africa, as well as in women, while it is decreasing among men. In Europe, Hungary, Serbia, and Turkey are the countries with the highest lung cancer incidence and mortality. Although France is a country with a high-income index, the incidence of tobacco smoking is one of the highest in Europe.

Lung cancer incidence trends in the United States parallel temporal trends of a decrease in smoking prevalence, as well as an increase in proportion of disease diagnosed at a localized stage.¹ In contrast, countries like Serbia report that the incidence of lung cancer has increased over the past three decades with 60% of cases currently diagnosed at advanced stage.²

In this issue of The Lancet Regional Health-Europe, Debievre and colleagues present the French lung cancer trends over a 20-year period, covering two previous assessments carried out in 2000 and 2010 (KBP-210, and KP-2010-CPHG, respectively), and the present analysis, the KBP-2020 CPHG study, encompassing 8999 new lung cancer patients diagnosed in 82 French nonacademic public hospitals.³ The trends in lung cancer at diagnoses in this 20-year French initiative documents that the proportion of women with new diagnoses of lung cancer increased to 36.8% in comparison to 24.3% in 2010 and 16.0% in 2000 ($p < 0.0001$). Also, the proportion of nonsmokers was higher in 2020, 12.6% versus 10.9% in 2010, and 7.2% in 2000 ($p < 0.001$). Moreover, differences are observed in lung cancer stage at diagnosis with an increase of advanced stage in 2020, at 57.7% versus 42.6% in 2000 ($p < 0.0001$).

The increment in proportion of women with lung cancer diagnosis in 2020 could reflect the incidence that many women took up cigarette smoking later than men,

and were slower to quit, as has happened in the United States.¹ The fact that still 57.6% of new diagnosed lung cancer patients have stage IV could be due to several causes, for example, many nonsmoker patients and those with minimal smoking history have advanced stage at diagnosis, which is probably related to subadjacent driver alterations in EGFR, ALK, ROS1, RET, MET and TRK.⁴ However, this higher rate of advanced stage at diagnosis in 2020, contrasts with data from the United States where the proportion of disease diagnosed at a localized stage increased from 17% during the mid-2000s to 28% in 2018 due to the implementation of screening programs in 2013,¹ while it is closer to data derived from the Serbian Register.²

The French study portrays a real-world picture of lung cancer incidence by gender and stage at diagnosis, paving the way to better understand such recalcitrant disease and undertake the registry of lung cancer molecular studies as part of routine clinical care. In this regard, the ASCO and Ontario Health (Cancer Care Ontario) have adopted living guidelines updated on a regular basis which could serve to change the clinical practice. The ASCO Living Guideline on therapy for stage IV NSCLC with and without driver alterations has recently been published.^{5,6} Notwithstanding, ablating lung cancer incidence and augmenting survival is a multi-tasked endeavor commencing with low-dose computed tomography (LDCT) screening programs⁷ that include individuals who have never smoked,⁸ and continuing with tumor molecular studies for the above-mentioned molecular subsets of NSCLC, as well as BRAF, ERBB2 mutations, NRG1 fusions, and the opportunity to treat KRAS G12C lung cancer patients.⁹ The novelties in cancer management spread hope for lung cancer patients, as demonstrated by the fact that 33.1% of unresectable stage III NSCLC patients receiving chemoradiotherapy and consolidation treatment with durvalumab (immune checkpoint inhibitor) remain alive and free of disease progression at 5 years.¹⁰ In the current study, the early mortality rate for stage IV patients is still very high, close to 30%. It would be interesting to know how many of these cases diagnosed in a critical situation had access to molecular diagnostic tests, which can be effective even in life-threatening situations.

The Debievre and colleagues' study³ gauging the lung cancer trends over a 20-year period epitomizes the collective efforts to improve clinical care with important treatment implications, in particular, in the advanced setting.

The Lancet Regional Health - Europe
2022;22: 100494
Published online xxx
<https://doi.org/10.1016/j.lanepe.2022.100494>

DOI of original article: <http://dx.doi.org/10.1016/j.lanepe.2022.100494>

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In the future, the 5-year mortality rate of this cohort will help us to understand if real-life data similarly reflects the impact that new therapies obtain in controlled phase III trials.

In summary, to decrease mortality from lung cancer, in addition to reducing tobacco consumption, other strategies are relevant, such as developing better drugs that block the neurotransmitter pathways involved in addictive behaviors, considering possible differences associated with gender, the earlier diagnosis through implantation of screening programs and the global access to molecular diagnosis and novel therapies.

Contributors

Dr Rafael Rosell had full access to all the data in the report and takes responsibility for the integrity of the data and the accuracy of the manuscript.

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Analysis, or interpretation of data: Drs R. Rosell and M. Gonzalez-Cao

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Statistical analysis: NA

Obtained funding: NA

Administrative, technical, or material support: Drs R. Rosell and M. Gonzalez-Cao

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Declaration of interests

The authors declare no conflicts of interest.

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