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Review

Long-term Survivors of Lung Cancer

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ABSTRACT

Introduction: Lung cancer (LC) is one of the most frequent tumors and remains the leading cause of cancer-related death. Improvements in treatment and the possible increase in cases diagnosed at early stages through screening programs mean that the number of long-term survivors of lung cancer is expected to increase.
Objective: To review the concept of long-term survival in lung cancer and the clinical, psychosocial, and follow-up needs of this growing population of patients.
Methods: A narrative review was prepared based on epidemiological data, clinical studies, and consensus documents on long-term survivors of lung cancer, particularly non-small cell lung cancer. The literature search was conducted across the PubMed, Scopus, and Cochrane Library databases. The search strategy employed MeSH terms and keywords including "Lung Neoplasms", "Survivors", "Long-Term Survivors", "Mass Screening", and "Primary Health Care", limited to articles published in English and Spanish.
Results: Survival is strongly conditioned by stage at diagnosis. There is no single definition of long-term survivor: in early-stage non-small cell lung cancer is usually defined as survival of 5 years or more, whereas in advanced or metastatic disease definitions vary between 18 months and 3 years. Long-term survivors may present recurrence or progression, second neoplasms, comorbidities related to smoking, immune-mediated toxicities, pain, fatigue, anxiety, depression, and difficulties in social and occupational reintegration.
Conclusions: The increasing number of long-term lung cancer survivors requires coordinated follow-up between primary care, hospital care, social and health services, patients, and families. Smoking cessation, management of comorbidities, physical exercise, psychological support, nutritional interventions, and monitoring of treatment-related toxicity should be integral parts of care.

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Supervivientes a largo plazo del cancer de pulmón

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RESUMEN

Introducción: El cáncer de pulmón (CP) es uno de los tumores más frecuentes y sigue siendo la principal causa de muerte relacionada con el cáncer. Las mejoras en el tratamiento y el posible aumento de casos diagnosticados en etapas tempranas mediante programas de cribado sugieren que se espera un incremento en el número de supervivientes a largo plazo de cáncer de pulmón.

Objetivo: Revisar el concepto de supervivencia a largo plazo en el cáncer de pulmón y las necesidades clínicas, psicosociales y de seguimiento de esta creciente población de pacientes.

Métodos: Se elaboró una revisión narrativa basada en datos epidemiológicos, estudios clínicos y documentos de consenso sobre supervivientes a largo plazo de cáncer de pulmón, en particular de cáncer de pulmón de células no pequeñas. La búsqueda bibliográfica se realizó en las bases de datos PubMed, Scopus y Cochrane Library. La estrategia de búsqueda empleó términos MeSH y palabras clave como "Neoplasias pulmonares", "Supervivientes", "Supervivientes a largo plazo", "Cribado masivo" y "Atención primaria de salud", limitándose a artículos publicados en inglés y español.

Resultados: La supervivencia está fuertemente condicionada por el estadio al momento del diagnóstico. No existe una única definición de superviviente a largo plazo: en el cáncer de pulmón de células no pequeñas en estadio temprano, generalmente se define como una supervivencia de 5 años o más, mientras que en la enfermedad avanzada o metastásica las definiciones varían entre 18 meses y 3 años. Los supervivientes a largo plazo pueden presentar recurrencia o progresión, segundos tumores, comorbilidades relacionadas con el tabaquismo, toxicidades inmunomediadas, dolor, fatiga, ansiedad, depresión y dificultades en la reintegración social y laboral.

Conclusiones: El creciente número de supervivientes a largo plazo de cáncer de pulmón requiere un seguimiento coordinado entre la atención primaria, la atención hospitalaria, los servicios sociales y sanitarios, los pacientes y sus familias. El abandono del tabaquismo, el manejo de las comorbilidades, el ejercicio físico, el apoyo psicológico, las intervenciones nutricionales y el seguimiento de la toxicidad relacionada con el tratamiento deben ser parte integral de la atención.

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1. MAIN TEXT

A family physician working in an urban setting will diagnose at least one lung cancer (LC) per year [1]. LC is one of the most frequent tumors, and it is estimated that in 2024, 32,768 cases were diagnosed in Spain (22,483 men), with 23,239 deaths (16,760 men) [2], representing one death every 20 minutes. LC is the third most commonly diagnosed type of cancer, after colon and rectal cancer and breast cancer, but it is the first in terms of number of deaths [3].

There is wide variability among provinces and autonomous communities, with the highest age-standardized incidence rates in Asturias (55.6 per 100,000 men; 16.0 per 100,000 women), the Basque Country (51.3 per 100,000 men; 17.1 per 100,000 women), Navarre (48.3 per 100,000 men; 15.6 per 100,000 women), and Castellón (48.8 per 100,000 men; 10.7 per 100,000 women). In contrast, the lowest incidence rates are observed in Granada (39.5 per 100,000 men; 8.6 per 100,000 women), La Rioja (39.3 per 100,000 men; 12.9 per 100,000 women), and Salamanca (41.7 per 100,000 men; 10.6 per 100,000 women) [4, 5].

The crude mortality rate in the period 2012-2021 was 54.5 deaths per 100,000 inhabitants (95.5 in men and 15.4 in women). From 2002 to 2022, the rate in men decreased by 28.1%, while in women it increased by 190.1% (Figure 1) [6].

A detailed analysis of Figure 1 provides crucial insights into the evolving trends of lung cancer mortality in Spain, cross-referenced by sex. The upper green line represents the absolute total of annual deaths, combining both men and women. This global indicator displays a steady historical increase driven by population growth and aging, followed by a stabilization phase in the most recent years.

However, the clinical and epidemiological core of the graph lies in the stark divergence between the two subgroups. The middle red line tracks the annual deaths among men. Following a historical peak, this trend demonstrates a clear, continuous downward trajectory from the 2010s onward, reflecting a substantial reduction in male tobacco consumption over the past decades [1, 2].

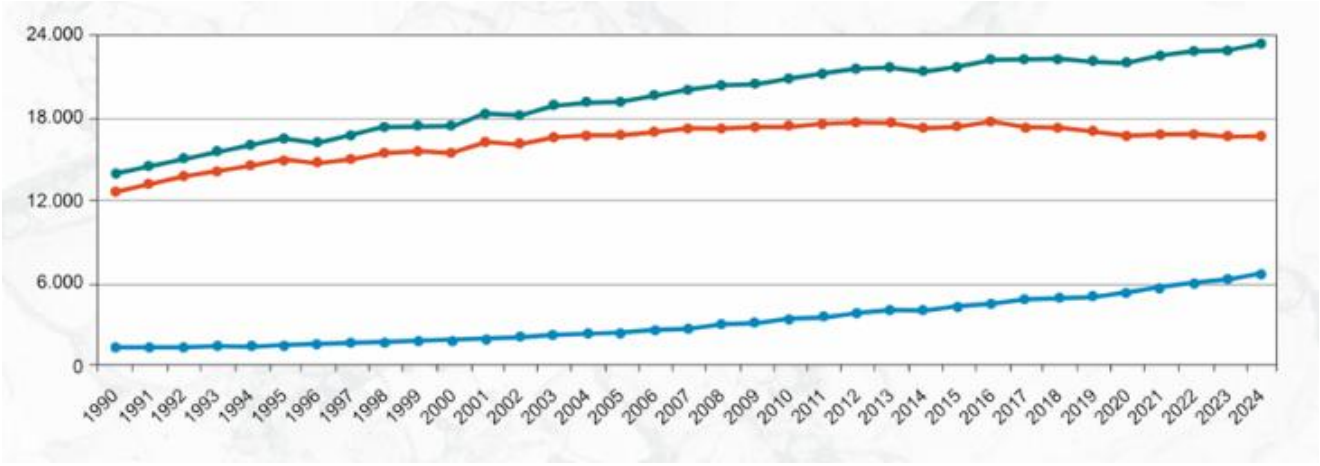

Figure 1: *Statistics on deaths according to cause of death: malignant neoplasm of the trachea, bronchi, and lung. Spain, 1990-2024.*

Conversely, the lower blue line represents the annual number of female deaths. This indicator displays an alarming and uninterrupted upward trend from 1990 through 2024. This sharp increase represents a critical epidemiological shift: due to the delayed incorporation of women into the smoking habit during the late 20th century, female lung cancer mortality has escalated to the point of surpassing traditional oncological milestones, such as breast cancer mortality [1, 3].

Mathematically, the stabilizing behavior of the upper total line is the direct result of these opposing forces: the progressive contraction of male deaths being counterbalanced by the aggressive surge in female mortality. Ultimately, this graphical breakdown highlights that while therapeutic advancements are successfully extending life expectancy, public health strategies must urgently deploy sex-specific prevention frameworks to curb the distinct expansion of the disease among the female population.

Non-small cell lung cancer (NSCLC) accounts for more than 85% of all LCs [7]. Survival is clearly conditioned by the stage at the time of diagnosis. Thus, it may reach 92% (stage IA1), compared with less than 1% in stage IVB [8]. Small cell lung cancer accounts for only 10-15% of all LCs and has much higher mortality. The median 2-year survival is less than 14% if the disease is limited, compared with 2-4 months if it is extensive, with 5-year survival figures below 2% [9]. More than 70% of patients diagnosed with NSCLC are diagnosed at stages that preclude surgery with curative intent, which implies 5-year survival rates of only 12% in men and 18% in women in our country [9, 10]. In relation to the 2002-2007 period, survival has improved by 13.4% in men and 8.6% in women [2, 5].

To fully understand these shifts in advanced stages, it is necessary to consider the role of molecular drivers and precision medicine. The identification of oncogenic drivers has radically rewritten the therapeutic approach and survival benchmarks. Patients presenting specific alterations benefit from targeted oral tyrosine kinase inhibitors (TKIs), bypassing the limitations of traditional cytotoxic chemotherapy. Similarly, the evaluation of programmed death-ligand 1 (PD-L1) expression guides the deployment of immune checkpoint inhibitors, which restore the patient's immune system capabilities against the tumor. To summarize these shifts, Table 1 maps the key biomarkers that primary care and specialized teams must track [11-13].

The increase in survival in LC, associated with the improvement of treatments and the possible increase in cases in initial stages due to the implementation of early detection programs [1, 14], means that there will be more long-term survivors with LC. These patients will require specialized follow-up coordinated among medical specialties.

Table 1: Biomarker Matrix and Therapeutic Impact in Advanced non-small cells lung cancer (NSCLC)			
Biomarker	**Approx. Prevalence**	**Targeted Guided Therapy**	**Clinical Survival Benefit / Impact**
EGFR Mutation	10-15%	Osimertinib, Erlotinib	Extends median survival beyond 3 years in metastatic disease.
ALK Rearrangement	3-5%.	Alectinib, Brigatinib, Lorlatinib	Achieves long-term remission; high central nervous system efficacy
KRAS	13-15%	Sotorasib, Adagrasib.	Provides a therapeutic option for a historically untreatable subgroup
PD-L1 Expression	Variable (≥50% high)	Pembrolizumab, Durvalumab	Drives long-term "tail-of-the-curve" survival in advanced stages.

To understand the ground-level reality of early detection and its direct correlation with the growing population of long-term survivors, the current status of screening implementation in Spain must be highlighted. The CASSANDRA project (Cancer Screening, Smoking Cessation AND Respiratory Assessment) is a multi-center public health pilot framework driven by the Spanish Society of Pneumology and Thoracic Surgery (SEPAR) in close alliance with 11 scientific societies and patient advocacy groups [1, 15].

Crucially, CASSANDRA does not view screening in clinical isolation; it integrates low-dose computed tomography (LDCT) directly with mandatory smoking cessation interventions and respiratory assessment through spirometry. Recent pilot data indicate that 77.51% of screened individuals present a negative baseline, 19.3% present indeterminate nodules requiring structured radiological tracking, and 3.19% result in a positive, early-stage cancer diagnosis—substantially shifting those individuals from an advanced palliative trajectory to a curable, surgical intervention [16].

Furthermore, to combat the national shortage of radiologists and handle the massive volume of imaging data, CASSANDRA incorporates advanced artificial intelligence (AI) reading software across its clinical network, minimizing errors and optimizing detection workflows. This real-world pilot evidence is essential for demonstrating the feasibility, clinical safety, and long-term cost-effectiveness required by the Ministry of Health to transform lung cancer from a fatal acute crisis into a highly manageable, chronic condition within the public health network [14].

Fitzhugh Mullan, co-founder of the National Coalition for Cancer Survivorship, as early as 1985 described what he called the “seasons of survival”, which included acute survival, or the period after diagnosis; extended survival, a time after completing treatment; and permanent survival, when recurrence seems very unlikely but the long-term effects of treatment continue [17].

However, there is no single criterion that identifies a patient as a long-term survivor. For early-stage NSCLC, it is defined as survival of 5 years or more [11]; for more advanced and metastatic stages, the literature varies between 18 months and 3 years [13]. A recent consensus document defines it as survival of 3 years or more and/or progression-

Table 2: Recurrence risk stratification in lung cancer (adapted from [29])		
Level of risk	**Clinical criteria**	**Follow-up recommendations**
Low risk	• Stage I. • Surgery without adjuvant therapy. • No significant comorbidities. • Non-smoker or low-risk former smoker.	• Visits every 6 months for 2 years; then annually. • Annual chest CT scan. • Annual evaluation of basic comorbidities. • Promotion of exercise, nutrition, and a healthy lifestyle.
Moderate risk	• Stages II-III treated with surgery + adjuvant therapy. • Mild or moderate comorbidities (mild COPD, hypertension, dyslipidemia) • Ex-smoker or moderate smoker	• Visits every 6 months (first 2 years); then annually until 5 years. • Chest TC scan every 6 months (first two years), then annually. • Evaluation and management of comorbidities (cardiovascular, respiratory, metabolic). • Intensive smoking cessation support.
High risk	• Stage III cancers treated with chemotherapy-radiotherapy +/- immunotherapy with curative intent. • Significant comorbidities (severe COPD, heart disease, complicated diabetes). • Active smoker. • Higher risk of secondary malignancies.	• Visits every 3-4 months (first 2-3 years); then every 6 months until 5 years, and annually thereafter. • Chest TC scan every 6 months (minimum 2-3 years). • Intensive monitoring of pulmonary, cardiovascular, and metabolic function. • Early management of late toxicities, including immune-mediated ones. • Pulmonary rehabilitation and psychosocial support when needed

COPD: Chronic Obstructive Pulmonary Disease; TC: Computed tomography.

free survival of 2 years or more [18].

Patients who have survived for some time after the diagnosis and treatment of cancer want to know their prognosis. Standard survival curves at the time of diagnosis include patients who die during the first years. Conditional survival analysis estimates survival while considering the previous condition of having survived for a period of time [19].

In general, patients who do not present excess conditional mortality have 5-year survival exceeding 95%, a situation that occurs in patients with colorectal cancer, cutaneous melanoma, or stage I breast cancer [20]. This does not occur in patients with NSCLC, in whom it never exceeds 91% for those aged 25 to 49 years and 77% for those aged 50 to 74 years. Among other causes, the factors that most influence these data are age, initial stage, and not quitting smoking [18, 21, 22]. Survival is better in women and when the tumor is an adenocarcinoma [9].

In addition, patients with LC have multiple comorbidities, partly conditioned by smoking, that reduce survival. A recent Portuguese study found that among long-term NSCLC survivors (defined as more than 5 years), up to 32% had relapse or disease progression and up to 15.2% developed another tumor, with these data being worse among those who did not quit smoking (23% of patients) [9, 23]. In any case, almost half of long-term LC survivors die from comorbidities or infections [22, 24].

Long-term survivors of LC have worse scores for pain, fatigue, physical activity, anxiety, and depression [26].

Several publications present contradictory data on the use of imaging techniques in these long-term survivors for the early detection of new tumors; therefore, intervention patterns outside usual practice cannot be objectively recommended. To resolve this ambiguity and optimize health resources, structured guidelines must dictate clinical follow-up. Primary care clinicians and specialists require an explicit roadmap regarding the timing and selection of diagnostics [25, 27].

Risk stratification is essential for defining the intensity and frequency of follow-up. Survivors are classified as low, medium, or high risk based on stage, treatment received, and comorbidities, allowing for the tailoring of the care model and resource allocation [28]. Table 2 summarizes the follow-up recommendations from a recent consensus [29].

The expected increase in the number of long-term survivors with LC will require coordinated intervention among the different medical specialties, social and health services, and the administration, with the essential collaboration of patients and families [30].

The document on long-term survivors of LC [9] reaches consensus, among others, on the following points:

- The integration of primary care and hospital care in the follow-up of long-term survivors is essential to optimize resources and ensure coordinated follow-up.
- The appearance of second neoplasms in long-term survivors of advanced lung cancer may have a significant impact on patients; therefore, good medical follow-up is necessary.
- In patients with advanced lung cancer undergoing immunotherapy, and in long-term survivors, it is important to consider the possibility that immune-mediated toxicities may develop as a result of treatment (Table 3) [1].
- Long-term follow-up in advanced lung cancer is associated with a lower risk of progression.
- Follow-up of long-term survivors of lung cancer should be carried out in primary care.

Table 3: Adverse effects associated with immunotherapy and targeted treatments (adapted from [1])

Drug	Adverse effect
Afatinib	Diarrhea, skin rash, stomatitis, and dry skin.
Alectinib	Anemia, myalgia, hyperbilirubinemia, photosensitivity, and weight gain.
Brigatinib	CPK elevation, cough, hypertension, and pneumonitis.
Durvalumab	Thyroid dysfunction and pneumonitis.
Lorlatinib	Hypercholesterolemia, hypertriglyceridemia, edema, and peripheral neuropathy.
Osimertinib	QT prolongation and decreased ejection fraction.
Sotorasib	Liver abnormalities, diarrhea, anemia, hepatitis, and hyponatremia.

- Returning to work and to the social environment may be a challenging process for long-term survivors of lung cancer, and it is important to provide support and resources to facilitate adaptation to a new normality in their lives [30].
- Physical exercise among survivors of advanced lung cancer has been shown to have positive effects on physical condition, quality of life, anxiety, and self-esteem.
- Psychological and cognitive care is essential to address the emotional and cognitive needs of long-term survivors of lung cancer and may help them cope with the challenges related to their disease.
- Sexual education, psychological support, or pharmacological measures are important means of addressing altered sexual function in long-term survivors of advanced lung cancer.

- Relapse in smoking is an important concern in long-term survivors of lung cancer and should be addressed through specific prevention and support interventions.
- Daily fatigue (asthenia or fatigue) is a common concern among long-term survivors of advanced lung cancer and should be addressed through pharmacological, non-pharmacological, and/or psychosocial therapies.
- Patients with advanced lung cancer experience psychological concerns, such as living with uncertainty, fear of cancer progression, and anxiety about medical evaluations.
- Implementing specific nutritional guidelines may help promote the health and well-being of long-term survivors of advanced lung cancer.
- Cognitive impairment is a concern among long-term survivors of advanced lung cancer treated with immunotherapy and may affect their daily functioning and quality of life.

A deeper contextual analysis reveals a significant clinical gap regarding how these toxicities directly compromise patient well-being and survivorship. Table 3 serves as an essential safety checklist, yet the presence of these chronic adverse events creates profound psychosocial friction and degrades treatment adherence. For instance, skin toxicities from EGFR inhibitors or chronic diarrhea from sotorasib are not merely biochemical events; they induce social isolation, anxiety, and physical discomfort. If primary care physicians do not proactively manage these lingering side effects, patients frequently undergo unauthorized dose reductions or complete abandonment of therapy, directly shortening survival. Therefore, survivorship care must integrate active toxicity management with psychological counseling, shifting from a reactive strategy to an integrated palliative approach that optimizes quality of life [31].

Furthermore, as the clinical paradigm changes, modern monitoring technologies are becoming central to post-treatment surveillance. Emerging technological approaches, such as liquid biopsies utilizing circulating tumor DNA (ctDNA), allow for the detection of molecular recurrence months before traditional radiological signs appear on a CT scan. Combined with advanced digital health tools and wearable remote monitoring systems, multi-disciplinary teams can now track patient-reported outcomes and early signs of pneumonitis or cardiovascular distress in real time, bridging the gap between home-based care and specialized hospital units [32].

2. CONCLUSIONS

First, it must be underscored that lung cancer, once considered an inevitably fatal and incurable disease, is now a chronic medical condition that necessitates long-term surveillance, much like diabetes or hypertension.

Second, managing this growing population successfully requires systemic collaboration not only from oncologists but from a comprehensive multidisciplinary network comprising family physicians, psychologists, dietitians, and social workers.

Third, evidence demonstrates that continuity of care must transcend the hospital environment, as the patient's domestic quality of life and family-centered support exert a direct impact on survival duration.

In short, the fight against lung cancer does not end with the eradication of the tumor; the real victory is won by reintegrating the survivor into society socially, physically, and mentally.

3. CONFLICT OF INTERESTS

The authors have no conflict of interest to declare. The authors declared that this study has received no financial support.

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