## Scientific letter

### Lung Cancer Diagnostic Delay Time and Related Variables

### *Demora diagnostica en carcinoma de pulmon: variables relacionadas*

*Dear Editor,*

In Spain, lung cancer (LC) is the third most common and leading cause of cancer-related death.[1] Its diagnosis requires several tests and takes time. Given that LC survival depends on the extension (cTNM stage) at the time of diagnosis and that a large percentage of cases are diagnosed in advanced stages, it is particularly important to know how long it takes to diagnose lung cancer in our environment. This is a matter that influences the patients' quality of life and emotional well-being; and is also regarded as an indicator of the healthcare quality.[2]

A multicentric observational descriptive study of patients diagnosed with LC in the Principality of Asturias (Spain) was carried out between January 1, 2022, and December 31, 2022, with the aim of analysing the diagnostic delay time and to study the factors that could influence it. Diagnostic delay (DD) was defined as the time (in days) between the first visit to a specialised care practice and the diagnosis of LC (including the cytohistological type and the extension), when a therapeutic decision is made.[3] All patients came from seven hospitals in the public healthcare system. Three centres had access to a multidisciplinary tumour committee (telematic in one of them) and only one had all the diagnostic and therapeutic procedures and equipment needed to manage LC. Three hospitals can carry out endobronchial ultrasound, being the reference for the rest of the hospitals for this technique. In one centre there was a fast-track lung cancer clinic. Data was collected on age, sex, comorbidity, cTNM stage and diagnostic tests; along with the time to complete LC diagnosis and staging.

A subgroup analysis was done in those patients in whom EBUS and PET-CT were performed, and the staging strategy employed was analysed, defined as PET-CT guided (first chest CT, followed by a PET scan and finally EBUS-TBNA) or EBUS guided (first chest CT, followed by EBUS-TBNA); the choice of strategy used in each centre was decided at their discretion. The study was approved by the Research Ethics Committee of the Principality of Asturias.

The comparison of proportions between groups was performed using the Chi-square test ($\chi^2$), with Fisher's bilateral test when the expected values were less than 5. For quantitative variables, Student's *t*-test or its non-parametric equivalent, Mann–Whitney *U*, were used. Variance analysis (ANOVA) was used to compare the average of three or more groups. A logistic regression analysis using DD as dependent variable and with the median value as cut-off point was done. A *p* value of less than 0.05 was considered to be significant.

Six hundred and thirty-two patients were collected, with a mean age of $67.8 \pm 14.51$ years. The mean diagnostic delay was $36.7 \pm 30.4$ days with a median of 29 days. Diagnosis and staging of LC were performed by pulmonologists in 494 patients (78.2%). As shown in Table 1, shorter DD was independently associated with TNM stage IV, fast-track lung cancer clinic, absence of comorbidity, hospital admission and hospital level of care 2 and 3.

In subgroup analysis, 186 patients were included, 98 with TMN stage I–IIIA and 58 IIIB–IIIC, the staging strategy was PET-CT guided in 131 patients and EBUS guided in 47; shorter DD was independently related with fast-track lung cancer clinic, EBUS-TBNA staging guided and absence of comorbidity (Table 1).

There are various guidelines on the desired times for the different steps in the diagnostic and therapeutic processes of LC. In our country, the National Health System's Cancer Strategy recommends a median of 15 days from the first appointment at the level of specialised care to the achievement of the pathological diagnosis (4 weeks if a molecular marker study is needed).[4] Our delay time is longer than this, so we believe that it is important to compare our findings with the data provided by previous studies. This comparison is difficult due to the lack of uniformity in the definition of the different delays and the expression of outcomes.[5] Furthermore, the comparison of our results with those obtained from other studies[2,6–10] was very heterogeneous (e.g. averages between 11 and 45 days for the diagnostic delay).

Regarding the factors that may determine the diagnostic delay in LC, TNM stage, fastrack lung cancer clinics, comorbidity, hospitalisation, and hospital level of care were related with it in our sample.

The different delays depending on the cTNM stage have also been shown in other articles,[2] where it was found that in a symptomatic patient with a more advanced disease, diagnostic studies are carried out more quickly and treatments are started earlier.[10] In this sense, our findings are similar with those described in other series, in which the diagnostic delay time was significantly longer in local stages.[2,11]

Comorbidity may prolong the time until diagnosis because more pre-treatment test are needed (such as functional evaluation) or clinical stability of the associated diseases is required for the initiation of treatment.

It may be assumed that the shortening of DD in hospitalized patients is related to a greater speed in carrying out the necessary studies, but this situation is influenced by other factors such as the existence of a early diagnosis clinics of LC or the availability and the order in which endoscopic techniques (bronchoscopy and EBUS) are performed[7]; in this regard, in a randomised controlled trial in which patients were assigned (1:1) to either conventional diagnosis and staging or EBUS-TBNA as an initial investigation after a staging CT scan, the median time to treatment decision was shorter in EBUS-TBNA group (14 days) than in conventional group

**Table 1**
Diagnostic delay and related variables.

| Variable | Univariate analysis | | Multivariate analysis | | |
|---|---|---|---|---|---|
| | DD (days) | p | OR | IC 95% | p |
| **All patients** | | | | | |
| *Comorbidity* | | 0.001 | | | |
| Yes | 39.24 ± 32.38 | | 1 | | |
| No | 30.55 ± 25.73 | | 0.63 | 0.42–0.94 | 0.02 |
| *c TNM stage* | | 0.0001 | | | |
| I–IIIA | 47.23 ± 35.87 | | 3.37 | 2.28–5 | 0.0001 |
| IIB–IIIC | 36.44 ± 23.94 | | 1.48 | 0.76–2.89 | 0.2 |
| IV | 29.42 ± 25.40 | | 1 | | |
| *Hospital admission* | | 0.0001 | | | |
| Yes | 27.34 ± 20.89 | | 0.29 | 0.19–0.43 | 0.0001 |
| No | 42.91 ± 35.01 | | 1 | | |
| *Fastrack LC* | | 0.0001 | | | |
| Yes | 24.86 ± 16.5 | | 0.28 | 0.15–0.52 | 0.0001 |
| No | 41.11 ± 33.67 | | 1 | | |
| *Hospital level of care* | | 0.001 | | | |
| 1 | 46.60 ± 41.81 | | 1 | | |
| 2 | 30.27 ± 21.76 | | 0.41 | 0.24–0.69 | 0.001 |
| 3 | 37.98 ± 30.44 | | 0.47 | 0.26–0.87 | 0.01 |
| *Histological type* | | 0.02 | | | |
| Adenocarcinoma | 36.73 ± 30.02 | | 1.26 | 0.23–6.71 | 0.78 |
| Squamous | 42.31 ± 34.43 | | 1.61 | 0.26–9 | 0.62 |
| Small cell | 30.21 ± 24.23 | | 1 | | |
| Others | 30.74 ± 33.51 | | 1.05 | 0.21–7.32 | 0.33 |
| *Type of specialist* | | 0.02 | | | |
| Pulmonologists | 34.88 ± 29.96 | | 1 | | |
| Others | 43.06 ± 32.88 | | 1.38 | 0.59–3.24 | 0.44 |
| **Subgroup analysis** | | | | | |
| *Comorbidity* | | 0.002 | | | |
| Yes | 28.01 ± 25.09 | | 1 | | |
| No | 21.74 ± 16.71 | | 0.33 | 0.15–0.72 | 0.001 |
| *Staging strategy* | | 0.01 | | | |
| EBUS guided | 22.11 ± 27.55 | | 0.28 | 0.11–0.67 | 0.005 |
| PET-CT guided | 34.32 ± 27.14 | | 1 | | |
| *Hospital admission* | | 0.0001 | | | |
| Yes | 20.58 ± 18.76 | | 1 | | |
| No | 29.80 ± 24.77 | | 0.76 | 0.39–1.47 | 0.4 |
| *Fastrack LC* | | 0.0001 | | | |
| Yes | 19.71 ± 14.13 | | 0.29 | 0.09–0.91 | 0.03 |
| No | 28.93 ± 25.21 | | 1 | | |
| *Hospital level of care* | | 0.01 | | | |
| 1 | 33.08 ± 31.61 | | 1 | | |
| 2 | 20.80 ± 16.60 | | 0.39 | 0.17–0.95 | 0.03 |
| 3 | 31.83 ± 22.10 | | 0.64 | 0.27–1.53 | 0.3 |

DD: mean diagnostic delay. Fastrack LC: fastrack lung cancer clinics. Subgroup analysis: patients in whom EBUS and PET-CT were performed.

(29 days).[12] Likewise, in our study, using an EBUS-guided staging strategy reduced DD, which might be especially useful for patients with local stages. It is surprising that in those hospitals with all the resources for diagnosis and staging (level 3), delay time is longer than in other intermediate level centres (level 2) that no have all these resources, which we believe could be due, among other factors, to the staging strategy employed, as shown by the fact that an EBUS-guided strategy was used in 14% of patients in level 3 versus 40% in level 2; all this reinforces the importance of staging strategy to ensure that the delay times are reasonable, and thus, in local and locoregional disease, EBUS-TBNA should be performed following the initial CT without waiting for PET results, in order to try to achieve this objective.

Our study has certain limitations. Firstly, as this is a multicentre observational study, the staging protocol may differ between centres, which could affect the final results; however, we would like to emphasise that our aim was to propose actions that could help to reduce delay times in our setting and one of them is undoubtedly the appropriate choice of the sequence of staging studies, which we believe is reasonably demonstrated by the results obtained. Second, we did not collect Primary Care delay times, which is an important part of the process, but we would like to point out that our initial

aim was to try to identify aspects of improvement in Specialised Care.

In conclusion, our diagnostic delay time is longer than desirable, even if they fall within the range provided by similar studies coming from similar healthcare areas. We believe that measures such as the process being carried out in fastrack diagnostic clinics and that the sequence of staging studies should be EBUS guided, especially in local stages, could help to improve the outcome.

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## Authors' contributions

Jesús Allende-González: conception, design, analysis, interpretation of data and drafting the work.

José Antonio Gullón-Blanco: analysis, interpretation of data and critical review of the intellectual content.

Juan Cascón-Hernández: critical review of the intellectual content.

Estela García-Coya, Eduardo Sánchez-Vázquez and Working Group of Asturian Society of Respiratory tract pathology (ASTUR-PAR): collection and contribution of data, final approval of the version to be published.

## Conflicts of interest

None.

## Appendix A. Working Group of Asturian Society of Respiratory tract pathology (ASTURPAR)

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