

Peer Review File

Article information: <https://dx.doi.org/10.21037/jtd-23-1494>

Reviewer A

I would like to commend the authors of this paper for discussing a key topic in patient care: quality of life. Often, mortality is used as a marker for treatment success, but the quality of life of survivors is equally necessary to know and much harder to study.

I have the following feedback to the authors.

Comment 1. Within the methods section, your study included all patients at least 5 years after treatment. Did this include patients actively undergoing treatment and if so, please clarify.

Reply 1: Our study included all patients who lived at least 5 years after the initial diagnosis (not treatment initiation) – line 73 to 75, regardless of whether they were on clinical and imaging surveillance or on active treatment. In fact, 6 patients were on active treatment at the time of the study (3 on TKI and 3 on immunotherapy). Changes in the text: No changes in the text.

Comment 2. Line 130- 31.8% of patients had disease progression/relapse- can this be broken down by initial staging?

Reply 2: We did the suggested analysis and included it in manuscript.

Changes in the text: Over a median follow up of 90 [78-106] months, 31.8% patients had disease progression or relapse (48% were stage I-II at diagnosis, 24% stage III and 28% stage IV). Page 8, line 137-138

Comment 3. In the discussion, there is mention of stage 1 vs 4 having no difference in quality of life scoring, however it would be interesting to see comparison tables of each stage and QoL scores

Reply 3: Thank you for the suggestion. We added the values into the text, as we had reached the maximum number of figures/tables.

Changes in the text: No other clinical or demographic characteristics, including stage IV at diagnosis, were statistically significant associated with worse QoL. However, the lowest score was found in stage IV LTLCS (61.52 in stage I-II; 63.43 in stage III and 52.78 in stage IV).

Reviewer B

Fonseca et al. performed a transversal study to identify characteristics associated with long-term survival (>5 years). They evaluated QoL and frequency of anxiety and depression among NSCLC patients treated from 2012 to 2016 in a specialized thoracic cancer institution in Portugal.

The study explores a population that has been poorly studied and may help to call attention to these patients since their number may increase soon due to improvements in screening and treatment patterns.

Major comments

Comment 1: The evaluation of QoL, as well as anxiety and depression, is somehow compromised by the fact there is no data regarding patients' status before diagnosis or treatment initiation, so it is difficult to ascertain what is their relationship with lung cancer. The authors should comment on that.

Reply 1: This is a great comment. Indeed, we do not know the QoL, anxiety and depression of these patients before lung cancer diagnosis. However, we do not assert a singular and direct relationship between lower QoL and lung cancer itself. Nevertheless, the literature shows that this population has a significant burden of other comorbidities and additional risk factors, which, together, can contribute to the lower QoL in this population. Studies in the literature evaluating QoL in a particular population rarely account for the patients' status before the evaluation at a specific point.

Changes in the text: No changes in the text.

Comment 2: Moreover, the authors should describe separately the characteristics of patients who died before 2022 to clarify if there was any difference from those still alive in 2022. They might have more aggressive diseases, which may bias positively the QoL assessment of the remaining patients.

Reply 2: This is an excellent suggestion. However, we intentionally chose not to provide that description due to the bias we might induce. It is known that not only the stage of the disease predicts the prognosis, but also its molecular characterization and the availability of innovative treatments. Between 2012 and 2016 significant progress was made regarding tumor characterization at diagnosis. For instance, only more recent diagnosed patients (close to 2016) underwent PD-L1 and NGS tests, making it challenging to compare these patients. Nevertheless, your suggestion is excellent for future studies.

Changes in the text: No changes in the text

Comment 3: Instead of grouping stage I and II together, these subgroups' frequencies should be depicted separately. I would guess most patients in this population will be classified as stage I.

Reply 3: For statistical purposes, we grouped stage I and II. Indeed, 81% of this group are stage I, leaving a small number of stage II patients. Therefore, we chose to group these patients with localized disease.

Changes in the text: No changes in the text.

Comment 4: How many patients who are still alive in 2022 are disease-free?

Reply 4: From the living patients in 2022, 83 patients (70.3%) were disease-free: 54 with stage I at diagnosis, 8 with stage II and 21 with stage III.

Changes in the text: Among LTLCS, 40 (25.3%) were dead at the time of the study, and from the living patients in 2022, 83 patients (70.3%) were disease-free: 54 with stage I at diagnosis, 8 with stage II and 21 with stage III. Page 8, line 142-143

Comment 5: I'd like to recommend excluding patients with typical and atypical carcinoids, as well as SCLC since these tumors have very different behavior from NSCLC.

Reply 5: This is an excellent point. However, our study aimed to analyze the PROs in lung cancer population. We do know that the prognostic varies significantly between histology; however, all these patients live with the burden of lung cancer diagnosis, impacting their daily routines and mental health. It would be interesting, with a significantly larger population, to analyze these histologic groups separately.
Changes in the text: No changes on the text.

The manuscript is well-written and may be of interest to the readers. It can be accepted for publication after the suggested adjustments have been made.