Palomar-Abril, V.; Soria-Comes, T.; Tarazona Campos, S.; Martín Ureste, M.; Giner-Bosch, V.; Maestu-Maiques, IC. (2020). Impact of Age on Inflammation-Based Scores among Patients Diagnosed with Stage III Non-Small Cell Lung Cancer. Oncology. 98(8):528-533. https://doi.org/10.1159/000506204

Clinical Study

Impact of Age on Inflammation-Based Scores among Patients Diagnosed with Stage III Non-Small Cell Lung Cancer

Short title	Inflammation-Based Scores in Stage III NSCLC

Vicente Palomar-Abril[a] Teresa Soria-Comes[a] Sonia Tarazona Campos[b] María Martín Ureste[a] Vicente Giner Bosch[c] Inmaculada Concepción Maestu Maiques[a]

[a]Department of Medical Oncology, Hospital Universitario Doctor Peset, Valencia, Comunitat Valenciana, Spain

[b]Genomics of Gene Expression Laboratory, Centro de Investigación Príncipe Felipe, Valencia, Comunitat Valenciana, Spain

[c]Department of Statistics and Operative Investigations,. ETSI Industriales,. Universidad Politécnica de Valencia, Valencia, Comunitat Valenciana, Spain

Corresponding Author: Prof. Vicente Palomar-Abril , Department of Medical Oncology, Hospital Universitario Doctor Peset, Av Gaspar Aguilar 90, Cuenca St. 138-5B, ES–46007 46017 Valencia (Spain), E-Mail vicente.palomar.abril@gmail.com

Additional Information: The study was conducted at Hospital Universitario Doctor Peset (Valencia, Spain).

Keywords Locally advanced non-small cell lung cancer; Inflammaging; Older patients; Prognostic Nutritional Index

Abstract

Background: Inflammatory and nutritional indexes are prognostic factors in non-small cell lung cancer (NSCLC). Furthermore, a low grade of chronic inflammation has been described in the older population (*inflammaging*). We aimed to evaluate the neutrophil-to-lymphocyte ratio (NLR), the Prognostic Nutritional Index (PNI), the advanced lung cancer inflammation index (ALI), the platelet-to-lymphocyte ratio (PLR), and the Glasgow Prognostic Score (GPS) in young and older patients diagnosed with locally advanced NSCLC to determine if significant differences between these groups exist.

Methods: We conducted a retrospective study analyzing the impact of age on the NLR, PNI, ALI, PLR, and GPS among patients diagnosed with stage III NSCLC at Hospital Universitario Doctor Peset between 2010 and 2015.

Results: We included 124 patients (84 young, 40 older patients). The median hemoglobin level and leukocyte count were lower in the older patients ($p = 0.0158$ and $p = 0.001$, respectively). A higher median C-reactive protein level was also found in this group ($p = 0.0095$). Regarding specific inflammatory indexes, the PNI, comprising inflammatory and nutritional parameters, was lower among the older patients ($p = 0.0463$). The median NLR, ALI, and PLR were similar in both age groups. Moreover, no differences between the age groups were found in the percentage of patients showing high versus low NLR (cutoff point, 5) or ALI (cutoff point, 18) or in the different GPS groups.

Conclusions: The baseline PNI, hemoglobin level, and lymphocyte count were lower among the older patients; furthermore, CRP was higher, possibly, because of a more prominent inflammatory status in older patients with lung cancer. No other immunological or nutritional analytical variables were different between the age groups.

Introductionintroduction

Lung cancer is one of the tumors with the highest mortality, accounting for more than 1.5 million deaths in 2012 [1]. Non-small cell lung cancer (NSCLC) is responsible for 85% of all cases [2]. In spite of all the progress in prevention and treatment, its prognosis is still poor, and overall survival is 15% 5 years after the diagnosis.

Stage III NSCLC occurs in a heterogeneous group of patients, leading to higher complexity in the choice of treatment due to differences in characteristics between populations included in clinical trials and patients seen in clinical practice. These variations are even greater if we consider older patients. According to the results of the study by Molina et al. [2], the median age at diagnosis of NSCLC is 70 years in Western countries; however, older populations are underrepresented in clinical trials, mainly because of their comorbidities [3, 4].

It is known that outcomes for patients diagnosed with cancer are determined not only by tumor characteristics but also by patient-related factors. During the last decade, the systemic inflammatory response has been demonstrated to play an important role in lung cancer development and progression [5]. Furthermore, the connection between cancer prognosis and nutritional factors has been studied during the last years [6]. Cachexia is commonly defined as involuntary weight loss secondary to an increased catabolism linked to inflammation [7]. The incidence of cachexia among patients diagnosed with NSCLC ranges from 18 to 28%. Moreover, precachexia is even more difficult to determine, because it is not always identified with the nutritional parameters usually employed. Van der Meij et al. [6] found precachexia in 23% of cases, and there is a growing interest in its early detection, because it is more effective to make an intervention to revert this process. For all these reasons, oncologists are concerned about the factors influencing lung cancer development, the

potential response to treatment, and the prediction of possible toxicities – especially in older patients, a more vulnerable population. Therefore, determining prognostic biomarkers is important in this type of tumor.

Several nutritional and inflammatory indexes have been studied as prognostic factors in stage IV NSCLC [8]: the neutrophil-to-lymphocyte ratio (NLR) [9–11], the Prognostic Nutritional Index (PNI) [12], the advanced lung cancer inflammation index (ALI) [13], the platelet-to-lymphocyte ratio (PLR) [14], and the Glasgow Prognostic Score (GPS) [8, 15, 16]. However, there is only scarce information about them with regard to stage III lung cancer, and it is unknown if there are differences in these parameters between young and older populations. Nevertheless, previous studies have reported a state of low-grade chronic inflammation seen in older individuals, named *inflammaging* [17]. That is why the aim of our study was to investigate if such differences between younger and older individuals exist among stage III NSCLC patients.

Subjects and Methodsmaterials|methods

Study Design

We performed an observational retrospective study, including patients diagnosed with locally advanced NSCLC (stage III) at Hospital Universitario Doctor Peset between 2010 and 2015. The patients were classified according to the guidelines of the Tumor-Node-Metastasis (TNM) staging system of the Union for International Cancer Control (7th edition) [18]. Patients older than 18 years with a histopathological diagnosis of NSCLC stage III were included, unless their clinical or laboratory data were not available. Patients were also excluded if they had been diagnosed with another tumor during the previous 3 months, or if an infection or acute complication was found at the moment of blood test acquisition, because this could have interfered with our results.

The clinicopathologic characteristics, comorbidities, and laboratory data (including neutrophil, lymphocyte, and platelet counts, as well as C-reactive protein [CRP], albumin, lactate dehydrogenase, and hemoglobin levels) were recorded before the patients received any treatment, and the data were archived in the hospital's informatics system. Functional status was assessed using the Eastern Cooperative Oncology Group (ECOG) scale, ranging from 0 to 5.

Inflammation-Based Rates and Scales

The NLR is defined as the absolute neutrophil count divided by the absolute lymphocyte count [19]. The PNI is an inflammatory and nutritional index, calculated with the formula 10 × albumin level (g/dL) + 0.0005 × lymphocyte count [9]. The ALI also evaluates the level of systemic inflammation, and it is the result of the operation body mass index (BMI) × albumin level (g/dL)/NLR; an ALI ≥18 indicates a low grade of inflammation and an ALI <18 a high grade of inflammation in the advanced setting [13]. The PLR is determined by the platelet count divided by the lymphocyte count. Finally, the GPS combines an inflammatory parameter (CRP) and a nutritional factor (albumin): patients are assigned 1 point if they have a CRP level >10 mg/L or hypoalbuminemia (<3.5 g/dL), and they are finally classified into groups with 0, 1, or 2 points [20].

Statistical Analysis

The patients were classified into two groups depending on their age, with the cutoff point set at 70 years. Their demographic and tumor characteristics are reported with descriptive statistics. Comparisons between the age groups for categorical variables were performed using the χ^2 independence test or Fisher's exact test. Continuous variables were compared between the two

groups using *t* tests, or the Wilcoxon rank-sum test if data were nonnormally distributed. $p < 0.05$ was considered statistically significant in all analyses.

Also, cutoff points for the NLR and ALI described in previous studies were used to categorize these variables into low/high NLR or ALI, in order to perform a comparison between their percentages among young and older patients using Fisher's exact test. For the PLR and PNI, no cutoff point has been clearly established; thus, only comparisons between medians or means were performed.

Results

Patients

A total of 124 patients with adequate medical information were analyzed. The demographic and tumor characteristics of the two groups are shown in Table 1. The patients ranged in age from 39 to 82 years (median age, 65.6). In both groups, most patients were male (79.8% in the young group and 90% in the older group) and had a current or former history of smoking habit. The predominant histology was squamous cell carcinoma in both groups (59.5 and 55% in the young and the older group, respectively). Also, more than half of the patients were diagnosed with stage IIIB NSCLC (52.4 and 57.5%, respectively). No statistically significant differences in demographic characteristics were found between the two groups.

BMI and Weight Loss

The median BMI was significantly lower among the young patients (25.37, vs. 27.91 kg/m^2 in the older group; $p = 0.0095$). However, the percentage of patients that had suffered from previous weight loss was similar in the two groups (28.5% in the young-adult group and 20% in the older patient group; $p = 0.3826$).

Blood Count

Levels of hemoglobin and lymphocytes were significantly lower in older patients (data shown in Table 2). Furthermore, the *p*-value for differences among neutrophil mean counts is shown to be close to the significance level ($p = 0.0622$).

Inflammation-Based Parameters and Indexes

The most generic parameter used as a laboratory inflammatory marker in clinical practice is the CRP level, which was shown to be statistically significantly higher among our older patients (median 53.1 mg/L [older] vs. 17.35 mg/L [young]; $p = 0.0096$).

Finally, we analyzed the inflammatory indexes in the young adults and older patients, and we found that the PNI, which encompasses nutritional and inflammatory information, was significantly lower among the patients aged ≥70 years (42.15 in the older patients vs. 45.19 in the young patients; $p = 0.0463$). The comparison is shown in Table 3 and Figure 1. A cutoff value for the PNI has not yet been definitively established, although values <45 have been proposed to be related to a worse prognosis.

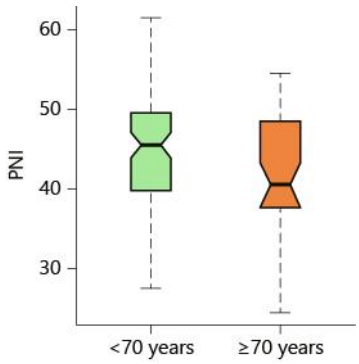

Fig. 1. Median Prognostic Nutritional Index (PNI) values for young and elderly patients (cutoff point, 70 years).

Nevertheless, no statistically significant differences were observed for the mean values of the NLR, PLR, and ALI or the percentage of patients in each GPS risk group (data summarized in Table 3). For the NLR, a cutoff point of 5 has consistently been reported to be related to prognosis [19]; thus, we dichotomized the variable to investigate if different proportions of patients showed a high NLR in the two groups, but this was not observed (as assessed with Fisher's exact test; $p = 1.00$). Similarly, the ALI was dichotomized using 18 as the cutoff point, and no difference was found (as assessed with the χ^2 test; $p = 0.5616$).

Discussion and Conclusions

The median age at diagnosis of NSCLC has been rising during the last years, being set in the last reports at 70 years [21]. Given the growing percentage of the population older than 65 years in Western countries, it may be predicted that the patients that we will treat in our clinical practice will probably tend toward an even older population.

It is widely known that with aging, several progressive changes in physiological systems and organs occur [22], as well as presumably in the tumor biology of older patients with cancer. Therefore, it is essential that this special subgroup of individuals is studied, and that we weigh different factors when we consider the possible therapies that our patients can be offered. Thus, we investigated the analytical and clinical parameters of patients diagnosed with stage III NSCLC to determine if significant differences exist between younger and older individuals, because this could help us in making treatment decisions.

Regarding demographic characteristics, no statistically significant differences were found between the two groups; however, a trend toward a higher percentage of patients with an ECOG performance status of 2 was seen in the group of patients aged 70 years or more, which could be due to a larger number and greater severity of comorbidities and functional impairment that are more frequently seen among older patients [23].

Among the clinical nutritional parameters, the BMI was significantly higher among the older patients; however, it is important to investigate other nutritional variables, because even obesity could still be present in patients suffering from malnutrition, protein deficiency, and also sarcopenia [24, 25]. That is why we cannot assume that being overweight sets aside the possibility of nutritional impairment. Thus, the BMI may not be an effective screening tool for malnutrition, especially among older patients with cancer, since these are often sedentary and typically have a lower muscular mass; that is why it was additionally evaluated with laboratory criteria.

Subsequently, we compared the basic analytical parameters, and we found that the hemoglobin level and lymphocyte count were lower in the older patients; furthermore, the older patients had a

significantly higher median CRP value than the younger patients. This illustrates the divergence in bone marrow reserve and hematological function between young adults and older patients and, interestingly, is also an indirect sign of inflammatory activity, which has also been reported in nononcological older populations [26]. Cancer is also a possible origin of higher CRP levels, but the patients in both our groups had the same diagnosis and no significant differences were found in the clinical stage of the tumor; therefore, the elevated level of that protein could be attributed to functional changes in aging.

Notwithstanding these data, no differences were observed in other inflammatory variables such as the neutrophil count, though a tendency toward having lower neutrophil levels was perceived among the older patients. Possibly, cancer could play a role in some of these changes, since differences in neutrophil count have not been reported in the general population [27]. Nevertheless, it is true that the neutrophil or lymphocyte count individually may have limitations in reflecting the inflammation or immune response in patients, which incited the development of indexes that comprise more than one of these values to have a better understanding of the inflammatory, immunological, and nutritional status of our patients.

Regarding the specific inflammation-based indexes, the PNI was found to be significantly lower among the older patients in our study. This parameter includes nutritional and immunological variables and therefore largely reflects the level of systemic inflammation and nutritional status, which both play critical roles in disease progression and prognosis in patients diagnosed with cancer [28]. Lower PNI values have been associated with worse outcomes in patients diagnosed with different types of tumors, including NSCLC, especially in the advanced setting [12, 29], and they have also been found to be related to older age and poorer ECOG performance status [30], but mainly in Asian populations. However, to our knowledge, only scarce data have been published in our area, and even less on localized-stage NSCLC.

One of the inflammatory indexes that has been widely reported as a prognostic factor in NSCLC and a marker for inflammatory response is the NLR [31, 32]; nevertheless, we found no differences in median NLR values between the older and the younger patients in our cohort. This could be due to a relatively small sample size; nonetheless, although a lower lymphocyte count was observed among the older patients in our study, there was also a trend toward a lower neutrophil count. That is why another possible explanation is that the high heterogeneity observed in older populations – since it is known that older patients differ substantially in their comorbidities, as well as in their cognitive, emotional, social, and functional status [33] – may not only influence laboratory parameters but also cancer outcomes and the toxicity of treatments.

The other indexes that we investigated (ALI, PLR, and GPS) were also similar in the two age groups. Although older patients are more prone to have poor nutritional and immunological conditions [27], cancer itself could also be related to systemic inflammation and impaired nutritional function. However, our findings could suggest that changes in the lymphocyte subpopulation and in albumin levels (and, therefore, in the indexes that are mainly based on these values) are more related to aging than neutrophil and platelet counts (and, subsequently, the ratios based on these parameters).

On the one hand, we would like to mention the limitations of this study, which include – besides the relatively small sample size – firstly, its retrospective nature, which was the origin of missing parameters for some of the variables, and, secondly, its basis on a single-center experience. However, interesting results could still be gained from our cohort, which should be confirmed in larger and multicenter series. On the other hand, we would like to outline the strengths of our research. Most of the immunological parameters in stage III NSCLC have been studied in Asian

populations; however, differences between Western and Eastern populations have been reported for several diseases, so information regarding this issue needed the assessment that we have performed. Moreover, investigations regarding differences between young and older patients diagnosed with lung cancer using laboratory parameters provide useful information based on reproducible and inexpensive explorations.

Taking all this together, we found that the nutritional and immunological status of older patients diagnosed with stage III NSCLC appears to be different from that of younger patients with the same diagnosis – particularly if inflammatory and nutritional parameters are taken into consideration together, as is the case with the PNI. As nutritional and immunological parameters have been associated with prognosis and outcome in patients diagnosed with lung cancer, our findings have clinical implications. Furthermore, the heterogeneity in the aging process makes it even more significant to assess clinical and laboratory parameters in a more exhaustive manner, including a comprehensive geriatric evaluation.

Statement of Ethics

The study was conducted in accordance with the Declaration of Helsinki and after having obtained approval from the institutional research ethics committee. Informed consent was waived due to the retrospective nature of the study and assured anonymity.

Disclosure Statementdisclosure statement

The authors have no conflicts of interest to disclose.

Funding Sources

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Author Contributions

V. Palomar-Abril designed the research, acquired the data, and contributed to data analysis and interpretation. He also prepared the first draft of the manuscript and edited and reviewed it. T. Soria-Comes designed the research and helped with data analysis and the preparation of the first draft of the manuscript. Moreover, she reviewed the manuscript and edited the final version. S. Tarazona Campos participated in the design of the statistical analysis and also performed it. Besides this, she reviewed the manuscript and edited the final version. V. Giner Bosch participated in the design of the statistical analysis and also performed it. Besides this, he reviewed the manuscript. M. Martín Ureste helped with the study design and data interpretation and also reviewed the manuscript. I.C. Maestu Maiques also conducted the study design, helped with data interpretation and the statistical analysis, and edited the final version of the manuscript. All authors approved the final version of the manuscript.

References

1. Wong MCS, Lao XQ, Ho KF, Goggins WB, Tse SLA. Incidence and mortality of lung cancer: global trends and association with socioeconomic status. Sci Rep. 2017;7:14300.http://dx.doi.org/10.1038/s41598-017-14513-7[check doi][Pubmed partial-vol, last-page, stl, first-page, iss, au3]

2. Molina JR, Yang P, Cassivi SD, Schild SE, Adjei AA. Non-small cell lung cancer: epidemiology, risk factors, treatment, and survivorship. Mayo Clin Proc. 2008;83:584–94.[not available]

3. Pallis AG, Gridelli C, Wedding U, Faivre-Finn C, Veronesi G, Jaklitsch M, et al. Management of elderly patients with NSCLC; updated expert's opinion paper: EORTC Elderly Task Force, Lung Cancer Group and International Society for Geriatric Oncology. Ann Oncol. 2014;25:1270–83.http://dx.doi.org/10.1093/annonc/mdu022[Crossref partial-stl, iss, atl]

4. Blanco R, Maestu I, de la Torre MG, Cassinello A, Nuñez I. A review of the management of elderly patients with non-small-cell lung cancer. Ann Oncol. 2015;26:451–63.http://dx.doi.org/10.1093/annonc/mdu268[Pubmed exact]

5. Hanahan D, Weinberg RA. Hallmarks of cancer: the next generation. Cell. 2015;144:646–74.http://dx.doi.org/10.1016/j.cell.2011.02.013[check doi][Pubmed partial-iss][Check Journal Title]

6. van der Meij BS, Schoonbeek CP, Smit EF, Muscaritoli M, van Leeuwen PAM, Langius JAE. Pre-cachexia and cachexia at diagnosis of stage III non-small-cell lung carcinoma: an exploratory study comparing two consensus-based frameworks. Br J Nutr. 2013;109:2231–9.http://dx.doi.org/10.1017/s0007114512004527[Crossref partial-iss]

7. Fearon K, Strasser F, Anker SD, Bosaeus I, Bruera E, Fainsinger RL, et al. Definition and classification of cancer cachexia: an international consensus. Lancet Oncol. 2011;12:489–95.http://dx.doi.org/10.1016/s1470-2045(10)70218-7[Crossref partial-stl, iss][Check Journal Title]

8. Pinato DJ, Shiner RJ, Seckl MJ, Stebbing J, Sharma R, Mauri FA. Prognostic performance of inflammation-based prognostic indices in primary operable non-small cell lung cancer. Br J Cancer. 2014;110:1930–5.http://dx.doi.org/10.1038/bjc.2014.145[Crossref partial-iss][Check Journal Title]

9. Kos FT, Hocazade C, Kos M, Uncu D, Karakas E, Dogan M, et al. Assessment of prognostic value of "neutrophil to lymphocyte ratio" and "prognostic nutritional index" as a sytemic [sic!] inflammatory marker in non-small cell lung cancer. Asian Pac J Cancer Prev. 2015;16:3997–4002.http://dx.doi.org/10.7314/apjcp.2015.16.9.3997[Crossref partial-stl, iss, atl][Check Journal Title]

10. Templeton AJ, McNamara MG, Šeruga B, Vera-Badillo FE, Aneja P, Ocaña A, et al. Prognostic role of neutrophil-to-lymphocyte ratio in solid tumors: a systematic review and meta-analysis. J Natl Cancer Inst. 2014;106:dju124.http://dx.doi.org/10.1093/jnci/dju124[check doi][Crossref partial-iss, au3, au6, atl]

11. Sacdalan DB, Lucero JA, Sacdalan DL. Prognostic utility of baseline neutrophil-to-lymphocyte ratio in patients receiving immune checkpoint inhibitors: a review and meta-analysis. Onco Targets Ther. 2018;11:955–65.http://dx.doi.org/10.2147/ott.s153290[check doi][Crossref partial-vol, stl, au3]

12. Wang Z, Wang Y, Zhang X, Zhang T. Pretreatment prognostic nutritional index as a prognostic factor in lung cancer: review and meta-analysis. Clin Chim Acta. 2018;486:303–10.http://dx.doi.org/10.1016/j.cca.2018.08.030[Crossref partial-stl][Check Journal Title]

13. Jafri SH, Shi R, Mills G. Advanced lung cancer inflammation index (ALI) at diagnosis is a prognostic marker in patients with metastatic non-small cell lung cancer (NSCLC): a retrospective review. BMC Cancer. 2013;13:158.http://dx.doi.org/10.1186/1471-2407-13-158[check doi][Crossref partial-iss, atl][Check Journal Title]

14. Zhao QT, Yuan Z, Zhang H, Zhang XP, Wang HE, Wang ZK, et al. Prognostic role of platelet to lymphocyte ratio in non-small cell lung cancers: a meta-analysis including 3,720 patients. Int J Cancer. 2016;170:164–70.http://dx.doi.org/10.1002/ijc.30060[check doi][Crossref partial-au6, vol, stl, iss, au4, au1, au5][Check Journal Title]

15. Miyazaki T, Yamasaki N, Tsuchiya T, Matsumoto K, Kunizaki M, Taniguchi D, et al. Inflammation-based scoring is a useful prognostic predictor of pulmonary resection for elderly patients with clinical stage I non-small-cell lung cancer. Eur J Cardiothorac Surg. 2015;47:e140–5.http://dx.doi.org/10.1093/ejcts/ezu514[Crossref partial-iss]

16. Proctor MJ, Morrison DS, Talwar D, Balmer SM, O'Reilly DS, Foulis AK, et al. An inflammation-based prognostic score (mGPS) predicts cancer survival independent of tumour site: a Glasgow Inflammation Outcome Study. Br J Cancer. 2011;104:726–34.http://dx.doi.org/10.1038/sj.bjc.6606087[Crossref partial-au5, iss][Check Journal Title]

17. Xia S, Zhang X, Zheng S, Khanabdali R, Kalionis B, Wu J, et al. An update on inflamm-aging: mechanisms, prevention, and treatment. J Immunol Res. 2016;2016:8426874.http://dx.doi.org/10.1155/2016/8426874[check doi][Crossref partial-vol, stl]

18. Mirsadraee S, Oswal D, Alizadeh Y, Caulo A, van Beek E Jr. The 7th lung cancer TNM classification and staging system: review of the changes and implications. World J Radiol. 2012;4:128–34.http://dx.doi.org/10.4329/wjr.v4.i4.128[check doi][Crossref partial-stl, iss][Check Journal Title]

19. Peng B, Wang YH, Liu YM, Ma LX. Prognostic significance of the neutrophil to lymphocyte ratio in patients with non-small cell lung cancer: a systemic review and meta-analysis. Int J Clin Exp Med. 2015;8:3098–106.[Pubmed partial-au2, iss, au3, au4]

20. Kobayashi S, Karube Y, Inoue T, Araki O, Maeda S, Matsumura Y, et al. Advanced lung cancer inflammation index predicts outcomes of patients with pathological stage IA lung adenocarcinoma following surgical resection. Ann Thorac Cardiovasc Surg. 2019;25:87–94.[not available]

21. National Cancer Institute. Surveillance, Epidemiology, and End Results Program. Cancer Stat Facts: lung and bronchus cancer. 2018. Available from: http://seer.cancer.gov/statfacts/html/lungb.html.[not available]

22. Zhang X, Meng X, Chen Y, Leng SX, Zhang H. The biology of aging and cancer: frailty, inflammation, and immunity. Cancer J. 2017;23:201–5.http://dx.doi.org/10.1097/00130404-201707000-00002[Crossref partial-stl, iss, atl][Check Journal Title]

23. Soto-Perez-de-Celis E, Li D, Yuan Y, Lau YM, Hurria A. Functional versus chronological age: geriatric assessments to guide decision making in older patients with cancer. Lancet Oncol. 2018;19:e305–16.http://dx.doi.org/10.1016/s1470-2045(18)30348-6[Crossref partial-stl, iss][Check Journal Title]

24. Zhang X, Sun M, McKoy JM, Bhulani NNA, Valero V, Barcenas CH, et al. Malnutrition in older patients with cancer: appraisal of the Mini Nutritional Assessment, weight loss, and body mass index. J Geriatr Oncol. 2018;9:81–3.http://dx.doi.org/10.1016/j.jgo.2017.07.012[Crossref partial-stl, iss]

25. Morel H, Raynard B, d'Arlhac M, Hauss PA, Lecuyer E, Oliviero G, et al. Prediagnosis weight loss, a stronger factor than BMI, to predict survival in patients with lung cancer. Lung Cancer. 2018;126:55–63.http://dx.doi.org/10.1016/j.lungcan.2018.07.005[Crossref partial-au6, au5, au4, au6, au5, au3, au4]

26. De Martinis M, Franceschi C, Monti D, Ginaldi L. Inflammation markers predicting frailty and mortality in the elderly. Exp Mol Pathol. 2006;80:219–27.http://dx.doi.org/10.1016/j.yexmp.2005.11.004[Crossref partial-last-page, stl, iss]

27. Maijó M, Clements SJ, Ivory K, Nicoletti C, Carding SR. Nutrition, diet and immunosenescence. Mech Ageing Dev. 2014;136–137:116–28.http://dx.doi.org/10.1016/j.mad.2013.12.003[Crossref partial-vol, stl, au1][Check Journal Title]

28. Zhang X, Meng X, Chen Y, Leng SX, Zhang H. The biology of aging and cancer: frailty, inflammation, and immunity. Cancer J. 2017;23:201–5.http://dx.doi.org/10.1097/00130404-201707000-00002[Crossref partial-stl, au5, iss, au3, au4, au3, au5, au4, atl][Check Journal Title]

29. Nozoe T, Ninomiya M, Maeda T, Matsukuma A, Nakashima H, Ezaki T. Prognostic nutritional index: a tool to predict the biological aggressiveness of gastric carcinoma. Surg Today. 2010;40:440–3.http://dx.doi.org/10.1007/s00595-009-4065-y[Crossref partial-iss][Check Journal Title]

30. Shimizu K, Okita R, Saisho S, Maeda A, Nojima Y, Nakata M. Preoperative neutrophil/lymphocyte ratio and prognostic nutritional index predict survival in patients with non-small cell lung cancer. World J Surg Oncol. 2015;13:291.http://dx.doi.org/10.1186/s12957-015-0710-7[Pubmed partial-last-page, first-page, iss][Check Journal Title]

31. Scilla KA, Bentzen SM, Lam VK, Mohindra P, Nichols EM, Vyfhuis MA, et al. Neutrophil-lymphocyte ratio is a prognostic marker in patients with locally advanced (stage IIIA and IIIB) non-small cell lung cancer treated with combined modality therapy. Oncologist. 2017;22:737–42.http://dx.doi.org/10.1634/theoncologist.2016-0443[Crossref partial-stl, iss, atl][Check Journal Title]

32. Desai SC, O'Grady K, Kalnicki S, Bodner WR III, Garg MK, Ohri N, et al. Prognostic value of neutrophil-to-lymphocyte ratio following chemoradiation therapy for stage III non-small cell lung cancer. Int J Radiat Oncol. 2017;99(Suppl):E451–2.[not available]

33. Mohile SG, Velarde C, Hurria A, Magnuson A, Lowenstein L, Pandya C, et al. Geriatric assessment-guided care processes for older adults: a Delphi consensus of geriatric oncology experts. J Natl Compr Canc Netw. 2015;13:1120–30.http://dx.doi.org/10.6004/jnccn.2015.0137[Crossref partial-stl, iss][Check Journal Title]

Table 1. Demographics and clinical characteristics of the young (<70 years) and older (≥70 years) patients

<!--Col Count:3-->	<70 years (*n* = 84)	≥70 years (*n* = 40)
Age, years		
Median (range)	65.5 (39–82)	
Sex, *n* (%)		
Male	67 (79.8)	36 (90.0)
Female	17 (20.2)	4 (10.0)

<!--Col Count:3-->	<70 years (*n* = 84)	≥70 years (*n* = 40)
Smoking status, *n* (%)		
Nonsmoker	2 (2.4)	5 (12.5)
Ex-smoker	30 (35.7)	22 (55.0)
Current smoker	52 (61.9)	13 (32.5)
ECOG performance status, *n* (%)		
0	15 (17.9)	9 (22.5)
1	62 (73.8)	23 (57.5)
2	7 (8.3)	8 (20.0)
Histology, *n* (%)		
Adenocarcinoma	32 (38.1)	17 (42.5)
Squamous carcinoma	50 (59.5)	22 (55.0)
Other	2 (2.4)	1 (2.5)
Clinical stage, *n* (%)		
IIIA	40 (47.6)	17 (42.5)
IIIB	44 (52.4)	23 (57.5)

Table 2. Mean values of the basic hematological parameters according to age

<!--Col Count:4-->	<70 years (*n* = 84)	≥70 years (*n* = 40)	*p* value
Hemoglobin, g/dL	13.2	12.3	0.0158
Neutrophils, cells/mm^3	6,531	5,790	0.0622
Lymphocytes, cells/mm^3	2,126	1,919	0.001
Platelets, cells/mm^3	294,259	279,500	0.4493

Table 3. Median values of inflammation-based indexes in the two groups depending on age

<!--Col Count:4-->	<70 years (*n* = 84)	≥70 years (*n* = 40)	*p* value
PNI	45.19	42.15	0.0463
NLR	3.42	3.41	0.7043
PLR	151.97	168.45	0.3035
ALI	31.90	32.93	0.8018
GPS, %			
0	25.4	4.6	
1	27.1	31.8	
2	47.5	63.6	0.107

For the GPS, percentages of patients according to the presence of risk factors are shown. PNI, Prognostic Nutritional Index; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; ALI, advanced lung cancer inflammation index; GPS, Glasgow Prognostic Score.