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THERAPEUTIC RESULTS AND PROGNOSTIC FACTORS OF STAGE III NSCLC: A POPULATION-BASED STUDY IN TUNISIA

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***Background*: Prognostic factors are crucial to guide patient's selection through therapeutic decisions and outcome prediction. *Aim*: To investigate prognostic factors associated with improved survival in stage III non-small cell lung cancer. *Patients and Methods*: We retrospectively reviewed clinical data of 88 stage III non-small cell lung cancer patients treated between 2010–2017. Multidisciplinary evaluation prior to therapy onset was mandatory. Univariate analyses and multivariate logistic regression were performed to identify factors associated with survival. *Results*: Median follow-up was 28 months, 56% of patients experienced recurrence. Median overall survival (OS) was 19 months. On univariable analysis, improved OS correlated with younger age ($p = 0.011$), better performance score (ECOG PS < 2) ($p < 0.01$), absence of weight loss ($p = 0.019$) and smaller tumor size ($\leqslant 7$ cm) ($p = 0.005$). OS was improved in patients receiving therapy planned by multidisciplinary meeting compared with those who did not ($p < 0.01$), in those with resected tumors ($p = 0.001$), responding to therapy (neoadjuvant chemotherapy ($p = 0.034$) and concurrent chemoradiation ($p = 0.001$), as well as those with lower neutrophil-lymphocyte ratio ($p = 0.026$) and lower platelet-lymphocyte ratio ($p = 0.003$). Postoperative adjuvant therapy increased OS (64 *vs* 24, $p = 0.025$). Longer recurrence-free interval, locoregional failure and better perfomance status at recurrence were good prognostic factors for OS. Multivariate analysis showed that only upfront surgery followed by adjuvant therapy (hazard ratio (HR) = 0.61; 95% confidence interval (CI) 0.38–0.96; $p = 0.034$), adherence to multidisciplinary team decision (HR = 0.26; 95% CI 0.15–0.47; $p < 0.01$) and tumor size > 7 cm (HR = 2.31; 95% CI 1.29–4.13; $p = 0.005$) were independent prognostic factors affecting OS. *Conclusions*: Optimal therapeutic strategy and adherence to the decision provided by the multidisciplinary evaluation of patients played an important role in stage III non-small cell lung cancer outcome.**
***Key Words:* NSCLC, fprognosis, stage III, management.**

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Lung cancer is widely spread around the world and remains a poorer prognosis disease compared to other cancers [1]. Every year more than 10 000 Tunisians die from lung malignancy, making it the first cause of cancer related death and the second in prevalence [2].

The medical community has been working for years to endorse new advances and innovations in order to improve its outcome and to further bend the lung cancer survival curves in particular for locally advanced tumors.

Management of stage III non-small cell lung cancer (NSCLC) is attracting widespread interest among radiotherapists, medical oncologists, thoracic surgeons and recently researchers in targeted therapies and immunotherapy. Management is nowadays multimodal with no single validated "Gold standard" [3]. Selecting the optimal therapeutic sequence with the better survival in stage III NSCLC patients remains a subject of current controversies. Several factors should be taken into account in strategy selection for stage III NSCLC such as age, weight loss, comorbidities as well as tumor histology, localization, dimensions, T extension and lymph node involvement [4].

Survival rates for this stage remained historically poor with a wide range in reported outcomes. Disparities in outcomes could be explained by heterogeneity in clinical features and diversity in therapeutic options [4–7]. Optimizing patient selection in the setting of multimodality treatment approach in stage III NSCLC is crucial to improve outcome and therapeutic results.

Several treatment-related factors were evaluated, and some were validated [8]. A number of studies have suggested several scores and indices to guide therapeutic decisions and predict outcome, such as Montreal prognostic score, lung cancer prognostic index score [9, 10] and the modified Glasgow Prognostic Score [11]. However, reported data remain conflicting and inconclusive without a general consensus on this issue. Moreover, most studies on prognostic factors tended to focus on metastatic lung cancer while few have addressed stage III NSCLC.

Few Tunisian studies have reported real-word data on therapeutic results and prognosis factors of NSCLC while none, to the best of our knowledge, has focused only on stage III tumors [12–14]. Management of NSCLC in Tunisia faces several challenges: multimodal treatment is not widely available, there is a lack of radiation therapy centers and very limited access to innovative therapies. This context is similar in many low- and middle-income countries [12]. Prognostic factors can be a cost-effective way to guide specialists in their decision making process.

Therefore, we sought to evaluate survival outcomes, prognostic factors in stage III NSCLC patients and to investigate therapeutic results of the multimodal treatment approach in Tunisia.

PATIENTS AND METHODS

Patients. We retrospectively collected data about 88 patients with histologically confirmed stage

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Abbreviations used: CCRT – concurrent chemoradiation; CI – confidence interval; CRT – chemoradiation; ECOG – Eastern Cooperative Oncology Group; HR – hazard ratio; NACT – neoadjuvant chemotherapy; NLR – neutrophil/lymphocyte ratio; NSCLC – non-small cell lung cancer; OS – overall survival; PFS – progression free survival; PLR – platelet/lymphocyte ratio; PS – performance status; UP.S – upfront surgery.

IIIA/B NSCLC over a 7-years period between 2011 and 2017. Histological diagnosis was obtained by either endoscopic, image-guided percutaneous biopsy or surgically. Only adenocarcinoma, squamous cell carcinoma, carcinosarcoma and large cell histological subtypes were considered. We only included patients with optimal work-up such as bronchoscopy, contrast-enhanced body computed tomography scan and cranial magnetic resonance imaging/bone computed tomography scan if needed. Positron emission tomography — computed tomography scan was not available in our country at the study period. Staging followed the recommendations of the 7th edition of the American Joint Committee on Cancer Guidelines. All patients were discussed at the lung oncology multidisciplinary meeting, where the stage was re-evaluated, and treatment decisions were recommended. Patients who suffered from another neoplasia at initial diagnosis or during follow-up were excluded. Patients with missing data on received therapy and/or follow-up were also excluded. We collected pre-treatment data regarding clinical, biological, radiological and histological features. Data about the received therapy, treatment toxicity and follow-up were also collected. Ethics approval was obtained from the hospital Research Ethics Committee.

Multimodal therapy. Upon presentation at the lung oncology multidisciplinary meeting, one of the following treatment strategies was proposed: upfront surgery (UP.S) followed by adjuvant therapy, neoadjuvant chemotherapy (NACT) followed by a radical treatment or definitive chemoradiation (CRT). Patients planned for NACT had to receive 3 to 4 cycles of platinum-based doublets then re-evaluated for surgical resection otherwise definitive CRT. Treatment modality was then discussed with each patient. All patients had at least one treatment modality atour university hospital, which is the largest lung cancer center in the country.

Follow up. In the first two years, patients were followed with a visit including physical examination and chest X-Ray every 3 months, a contrast-enhanced body computed tomography scan every 6 months. A further brain magnetic resonance imaging and/or bone scan were performed if clinically indicated. Smoking cessation was offered to all patients. Disease progression must have been documented by radiological examinations. Biopsy was not mandatory for all patients. Progression free survival (PFS) was defined as the time between the date of pathologic diagnosis and disease progression (loco-regional or distant metastasis) or death, whichever occurred first. Overall survival (OS) was calculated from the time of pathologic diagnosis until death or last follow-up appointment (phone call follow up June 2019). Data about disease progression: clinical aspect, recurrence time and patterns were collected.

Statistical analysis. Continuous variables are presented as mean ± standard deviation or median (Q1 to Q3). The independent Student's *t*-test was used to assess statistical significance of difference between the groups (validity assumptions were satisfied). If the distributions were highly skewed, Mann — Whitney *U* test was utilized to test for differences. Categorical variables are presented as frequency (percentage). These variables were tested using the chi-squared test, except for out-migration, which was tested using Fisher's exact test. All tests of significance were two tailed, and *p*-values of 0.05 were considered significant.

Survival curves were generated using the Kaplan — Meier method and the log-rank test are used to compare patient groups.

Univariate and multivariate logistic regression were performed to identify factors associated with survival. Significant factors from the univariate analyses were included in the multivariate analyses according to the Cox regression descending step method. As first step, we introduced all factors with $p < 0.05$ and those between 0.05 and 0.25 in the univariate analysis, from step to step we removed the factor with the least «p» significance. Multivariate analysis made it possible to calculate adjusted relative risks, measuring the specific role of each factor. All statistics were performed with IBM SPSS version 25.

RESULTS

Population. During the study period, 88 patients met the required eligibility criteria. Median age was 62 years (Q1 53, Q369) and 24% of the population was over the age of 70. Eighty-two per cent were men and 85% were current active smokers with a median of 50 pack-years smoking (Q1 35, Q3 70). Half of the patients (51%) had at least one comorbidity. The majority of patients had an Eastern Cooperative Oncology Group performance status (ECOG PS) < 2 (84%) and no weight loss (63%) in the past 3 months (⩾ 10% of weight). Fifty-two per cent had significant chronic comorbidities, most reported ones were hypertension (21%), diabetes (17%) and pulmonary diseases; mainly chronic obstructive pulmonary disease (15%). The incidence of comorbidities was significantly higher in the > 70 years-group ($p = 0.002$).

Most common symptom at disease-onset included chronic cough (68%), followed by chest pain (52%), hemoptysis (39%) and dyspnea (34%). Stage IIIB patients were most likely to have dyspnea ($p = 0.02$) and hoarseness ($p = 0.035$).

Stage was equally distributed between IIIA and IIIB, with 9% IIIA-N0, 14% IIIA-N1, IIIA-N2 and 33% IIIB-N2, 17% IIIA-N3. Four Pancoast tumors were identified. Adenocarcinoma was the most common histological subtype (55%) followed by squamous cell carcinoma (44%) and large-cell carcinoma (1%). Adenocarcinoma occurred mainly in women ($p = 0.002$) and non-smokers ($p = 0.012$) compared with other subtypes. 24% of tumors were poorly differentiated.

Therapy outcomes. After the MDT discussion, planned therapy was NACT in 60%, UP.S in 20% and CRT in 20%. All patients planned for surgery were operated. Surgery was microscopically incomplete (R1) in 3 patients and 3 cases of unforeseen N2 involvement were reported. Adjuvant chemotherapy was given to all this subgroup, 17/18 patients had the indication

of postoperative radiation due to N2 disease and/or R1 resection. However, 7 patients couldn't complete their radiotherapy; main reasons were patient's refusal (n = 2), disease progression (n = 2), lost to follow-up (n = 2) and long delay of radiation onset (n = 1).

Patients proposed for NACT, had at least 3 courses of platinum-based regimen as intended. Twenty-two patients (42%) had a partial response to induction therapy, 14 patients (27%) had stable disease, and 9 patients (17%) had progressive disease. 5 cases were lost to follow up with 2 reported toxic deaths. Of 36 cases discussed for a second time at the lung oncology multidisciplinary meeting, the therapeutic decision was UP.S in 13, CRT in 25 and best supportive care in one. Still only 20 patients completed the planned treatment.

Among patients proposed for definitive CRT, 10/18 completed their treatment as planned. The majority (60%) had sequential chemotherapy that consisted of 2 to 4 courses of platinum-doublets followed by radiotherapy delivered to the tumor volume at a daily dose of 2 Gy to a total dose of 60 Gy over 6 weeks.

Disease progression and patterns of failure. During the observation period, 49 patients had disease progression (56%). The initial proposed strategy (UP.S/NACT/CRT) did not affect disease progression incidence ($p = 0.2$).

UP.S group. Half (n = 9/18) of the operated patients experienced progressive disease: local-regional (n = 2) and distant (n = 7). Of those who experienced distant failure, liver relapse was the most common (n = 4) followed by brain disease (n = 3). Median time to progression after surgery was 16 months (Q1 10, Q3 27). This delay was shorter in patients who had an incomplete R1 resection (9.5 *vs* 18 months, $p = 0.2$) without reaching statistical significance. 44% of patients declined their PS (ECOG $\geqslant 2$) at the time of disease progression.

NACT group. We noted that 33/52 (64%) had progressive disease. Of whom, 46% (n = 15) presented with loco-regional failure without evidence of distant metastases. 12 of 18 patients with metastatic disease had more than one site involved. For all patients, the most common site of failure was the lung (n = 26) followed by the brain (n = 9), bone (n = 4), adrenal glands (n = 4) and the liver (n = 2). Sixty percent of patients declined their PS (ECOG $\geqslant 2$) at the time of disease progression. Median time between the end of induction therapy and disease progression was 4 months (Q1 1, Q3 13). Choice of platinum (carboplatin/cisplatin) did not influence this delay nor the type local treatment received upon induction therapy. However, therapeutic discordance between the planned strategy and the administered treatment significantly shortened the delay of progression (2 *vs* 15 months, $p < 0.01$).

CRT group. 7 of 18 patients had progressive disease (39%). Disease failure was local in two cases. 3 of 5 patients with metastatic involvement had more than one organ involved. In order of frequency, recurrence sites were lung (n = 5), bone (n = 2), skin, adrenal gland and brain (n = 1). The median delay of disease progression was 3 months (Q1 1, Q3 6). 86% of patients declined their PS (ECOG $\geqslant 2$) upon disease progression.

Salvage therapy of progressive disease consisted of palliative chemotherapy alone (n = 29), CRT (n = 5) and best supportive care in 5 cases. Cranial irradiation was delivered in 3 cases alone and associated to chemotherapy in 7 cases. ECOG PS at recurrence ($p < 0.01$), presence of significant chronic comorbidities ($p = 0.03$) influenced significantly the choice of salvage treatment while failure pattern ($p = 0.2$) and initial weight loss ($p = 0.09$) did not.

Survival and prognostic factors. Median follow-up of the entire cohort was 28 months. Median PFS was 11 months. Estimated PFS rates at 1, 3 and 5 years were 45%, 21% and 13% respectively. The 1, 3 and 5-year OS rates were 68%, 30% and 25% respectively, with a median survival of 19 months. Several prognostic factors for OS and PFS were evaluated. Based on the log-rank test, no significant impact on OS nor PFS was reported for the following factors: smoking status, gender, chronic comorbidities, stage, histological sub-type, tumor grade, radiation therapy dose, type of local therapy after NACT. We evaluated several inflammatory markers. Median neutrophils/lymphocytes (NLR) ratio was 2.6 (Q1 1.65, Q3 4.14). When taking a cut off of 3, univariate analysis showed that higher NLR was significantly associated with worse OS (12 in NLR $\geqslant 3$ *vs* 21 in NLR <3, $p = 0.026$) and worse PFS (6 in NLR $\geqslant 3$ *vs* 13 in NLR < 3, $p = 0.007$).

Median platelet/lymphocyte ratio (PLR) was 155 (Q1 111, Q3 234). The cut-off value determined by ROC curves for PLR was 150. Higher PLR was significantly correlated with poorer OS (12 in PL $\geqslant 150$ *vs* 26 in PLR <150, $p = 0.003$) and PFS (7 in PLR $\geqslant 150$ *vs* 18 in PLR < 150, $p = 0.001$). Median lymphocyte-to-monocyte ratio was 3.6 (Q1 2.5, Q3 6.4). We failed to show that lymphocyte-to-monocyte ratio significantly influenced PFS nor OS ($p = 0.5$).

Longer recurrence-free interval > 6 months, (64 *vs* 12 when interval < 6 months, $p < 0.001$), loco-regional failure (local = 29 months *vs* distant = 18 months, $p = 0.019$) and better ECOG PS at recurrence (PS = 0–129 months *vs* PS $\geqslant 211$ months, $p < 0.001$) were significant good prognosis factor impacting OS. While type of salvage therapy ($p = 0.2$), multiplicity of failure site ($p = 0.1$) and multiple lines of salvage treatments ($p = 0.16$) did not affect OS.

In the Cox regression analysis, the model demonstrated the association of tumor size greater than 7 cm (hazard ratio (HR) = 2.31; 95% confidence interval (CI) 1.29–4.13; $p = 0.005$), UP.S followed by adjuvant therapy according to therapy planned according to multidisciplinary evaluation (HR = 0.61; 95% CI 0.38–0.96; $p = 0.034$) and adherence to the decision by multidisciplinary meeting (HR = 0.26; 95% CI 0.15–0.47; $p < 0.01$) as independent prognostic factors for OS (Figure). In this model, recent weight loss was borderline significant ($p = 0.085$), with the patients with weight loss having the trend toward a worsened survival (HR = 1.66; 95%CI 0.93–2.98). Survival was

not significantly influenced by stage of disease, smoking status, PS, age, and which platinum-salt were used in this model.

DISCUSSION

The present study investigated therapeutic results and prognostic factors of multimodal treatment of stage III NSCLC. We showed the important impact of the adherence to the therapy mode decided by multidisciplinary meeting on survival. Tumor size and surgery were also independent prognostic factors. Disease progression was observed in more than half of the patients (56%) within a relatively short time, and wide difference according to different therapeutic groups (16 months in UP.S, 4 months in NACT and 3 months in concurrent CRT (CCRT)).

PFS was 21% at 3 years, 13% at 5 years with a median at 11 months. Our results rated close to those reported in clinical trials of stage III NSCLC [15–17]. The highest PFS was observed in the PACIFIC trial with maintenance Durvalumab after CCRT reaching 16.8 months [18]. Despite multimodal therapy and multidisciplinary meeting evaluation, we observed a 1, 3 and 5-years OS rates of 68%, 30% and 25% respectively, with a median survival of 19 months. OS was worse compared to what is reported in the literature [7, 19, 20], the SEER database reported 34% OS at 5 years [21]. In countries with limited resources, multimodal treatment faces several challenges, explaining the jeopardized OS. Wide disparities exist between countries in terms of therapeutic results of NSCLC, especially in Africa [22, 23]. Furthermore, most reported series included other disease stages like I and II, while the stage III (exclusive in the present study) remains the most complicated group, with complex treatment strategies and worse outcome [24, 25].

There is an obvious need for prognostic factors in stage III NSCLC, in order to overcome heterogeneity and define more homogeneous groups who can benefit from appropriate treatment and more personalized clinical trials design. As expected, in the literature, reported prognostic factors are various and heterogeneous [8]. Conventional factors like age with a threshold of 70 years, weight loss and general condition before the start of treatment are redundant is different series [5, 6, 8, 26]. More "specific" factors were reported like tumor size that was shown to be independent in our series. Tumor size with a threshold of 7 cm, independently from stage IIIA/IIIB significantly impacted OS and PFS. The relationship between tumor size and outcome of NSCLC was previously highlighted in robust data from SEER database and from IASLC staging project [27]. They described bad impact in node negative and locally advanced node positive NSCLC, mainly treated with CRT only or UP.S only. Conversely to previous study, tumor size was independent factor despite different treatment modality from surgery to definitive CCRT in our population. As reported in previous findings in different cancer types, inflammatory markers such as NLR and PLR are an example of accessible and cost-effective prognostic factors that may be used to predict outcome in stage III

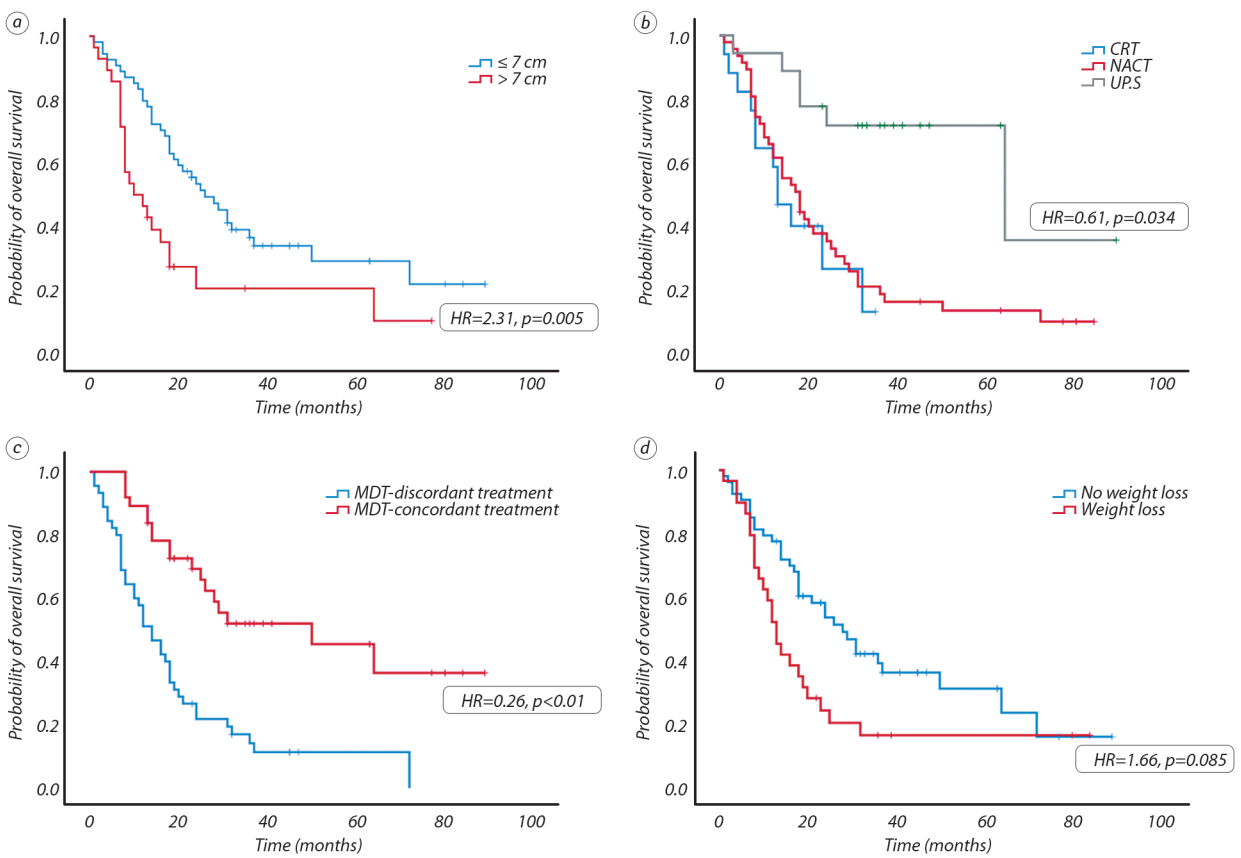

Figure. OS for patients according to tumor size with a cut-off of 7 cm (*a*), initial therapy strategy (*b*), adherence to multidisciplinary evaluation decisions (*c*) and to initial weight loss (*d*)

NSCLC patients. NLR and PLR but not lymphocyte-to-monocyte ratio appeared to be significant OS predictors in our cohort. Our findings were in line with those reported by Tong *et al.* [28], Yılmaz *et al*. [29] and Abril *et al*. [30]. These papers proved that these ratios could be considered as prognosis factors however, consensus on cut-off values lacked deeply.

As for the therapeutic component, the dose of radiotherapy, the treatment modality as well as the response to treatment (to NACT or CRT) have been considered by some authors as prognostic factors. Urvay *et al*. [6] demonstrated that a dose of radiotherapy ⩾ 60 Gy (without exceeding 74 Gy) significantly improved ($p < 0.001$) OS and that in the multivariate analysis, a dose ⩾ 60 Gy was an independent prognostic factor (HR: 0.3; 95% CI: 0.1–0.5; $p < 0.001$) which is consistent with the literature. In the present study, univariate and multivariate analysis showed that the initial therapeutic strategy based on UP.S and adherence to therapy mode planned by multidisciplinary meeting were independent significant prognostic factors, which goes hand in hand with the literature [28–30]. Operated patients seem to have better survival regarding earlier stage and better radical therapy [7]. Furthermore, patients referred to adjuvant chemotherapy and/or radiation therapy remain in good general condition without post-operative morbidity, which associates them with better outcome. It is now recognized that all efforts should be made to endorse the planned strategy of NSCLC management since non-adherence is one of the major negative prognostic factors [31–33].

The present study has some strengths. It included the unique group of stage III, reviewed within an MDT, such a group is already heterogeneous and have specific prognostic factors. Despite the small sample size, we were able to determine several important correlations. The current data reflect a real-world data about stage III NSCLC management in a limited resources country such as Tunisia and showed important features to focus on including optimal staging before surgery and adherence to MDT-planned therapy. Some pitfalls must be highlighted, though. This is a retrospective study, with a small-size and heterogeneous sample; some relevant factors couldn't be evaluated for lack of power. Positron emission tomography — computed tomography scan plays an important role in stage III NSCLC staging and none of our patients had positron emission tomography — computed tomography scan for work-up due to cost and limited availability.

In conclusion, findings of the current study highlighted the heterogeneity of stage III NSCLC in terms of clinical features, patterns of care and therapeutic results. Several pre-treatment factors such as age, ECOG PS, recent weight loss and tumor size were proved to affect survival. The adherence to planned treatment had high impact on outcome.

While developed countries are endorsing the use of new biological and metabolic variables as predictive and prognostic factors within prospective trials, low-income countries are left with cost-effective prognostic markers to guide patients' selection to optimal approaches in stage III NSCLC. These stage III-tailored prognostic factors evaluated in our paper are simple yet effective, hence they could be considered as a support-system for decision-making in limited-resources countries such as Tunisia.

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РЕЗУЛЬТАТИ ЛІКУВАННЯ ТА ПРОГНОСТИЧНІ ФАКТОРИ НДКРЛ III СТАДІЇ: ПОПУЛЯЦІЙНЕ ДОСЛІДЖЕННЯ В ТУНІСІ

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Стан питання: Прогностичні фактори мають вирішальне значення для відбору пацієнтів під час прийняття терапевтичних рішень і прогнозування результатів лікування. ***Мета:*** Дослідити прогностичні фактори, пов'язані з кращою виживаністю при недрібноклітинному раку легень III стадії. ***Пацієнти та методи:*** Ми ретроспективно проаналізували клінічні дані 88 пацієнтів з недрібноклітинним раком легень III стадії, що були проліковані в період з 2010 до 2017 р. Перед початком терапії обов'язково проводилося міждисциплінарне обстеження. Для виявлення факторів, асоційованих з виживаністю, було проведено однофакторний аналіз і множинну логістичну регресію. ***Результати:*** Медіана спостереження становила 28 міс, рецидиви були виявлені у 56% пацієнтів. Медіана загальної виживаності (ЗВ) склала 19 міс. За допомогою однофакторного аналізу встановлено, що краща ЗВ корелювала з більш молодим віком ($p = 0.011$), кращим загальним станом хворого (< 2 за шкалою ECOG PS) ($p < 0.01$), відсутністю втрати маси тіла ($p = 0.019$) і меншим розміром пухлини (⩽ 7 см) ($p = 0.005$). Рівень ЗВ був вищим у пацієнтів, що отримували терапію, заплановану за результатами міждисциплінарного консиліуму, у порівнянні з тими, хто отримував лікування, призначене з використанням іншого підходу ($p < 0.01$); у пацієнтів з резектованими пухлинами ($p = 0.001$), які відповіли на терапію (неоад'ювантна хіміотерапія ($p = 0.034$) і одночасне хіміопроменеве лікування ($p = 0.001$), а також у пацієнтів з більш низьким співвідношенням нейтрофіли-лімфоцити ($p = 0.026$) та більш низьким співвідношенням тромбоцити-лімфоцити ($p = 0.003$). Післяопераційна ад'ювантна терапія збільшила ЗВ (64 проти 24 міс, $p = 0.025$). Більш тривалий безрецидивний період, локорегіональна недостатність і кращий загальний стан хворого при рецидиві були позитивними прогностичними факторами ЗВ. Багатофакторний аналіз показав, що тільки попередня операція з подальшою ад'ювантною терапією (відношення ризиків (HR) = 0.61; 95% довірчий інтервал (CI) 0.38–0.96; $p = 0.034$), дотримання лікування, запланованого за результатами міждисциплінарного консиліуму (HR = 0.26; 95% CI 0.15–0.47; $p < 0,01$) і розмір пухлини > 7 см (HR = 2.31; 95% CI 1.29–4.13; $p = 0.005$) були незалежними прогностичними факторами, що впливають на ЗВ. ***Висновки:*** Оптимальна терапевтична стратегія і дотримання лікування, запланованого за результатами міждисциплінарного консиліуму, відіграють важливу роль у результатах лікування пацієнтів з недрібноклітинним раком легень III стадії.

Ключові слова: НДКРЛ, прогноз, III стадія, ведення хворих.