OUTCOME AND PREDICTING CHEMOTOXICITY IN ELDERLY PATIENTS WITH ADVANCED NON-SMALL CELL LUNG CANCER

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ABSTRACT

Introduction: *The global rise in aging population led to the increase of the number of elderly patients with lung cancer. Due to the impairment of the function of multiple organs, the work-up and treatment NSCLC for older patients become more difficult than adults. Because of lacking data about the characteristics of NSCLC in older patients, we conducted this study with the aims:*

Objectives

- To describe clinical, subclinical features and treatment of NSCLC in elderly patients.

- To evaluate the ability of predicting chemotoxicity of CARG score.

- To evaluate the efficacy of chemotherapy by the Progression-Free Survival.

Patients & method: *A retrospective study was conducted in a cohort of 26 patients older than 60, diagnosed with advanced NSCLC and treated by chemotherapy at least 3 cycles at Hue University Hospital from 1/7/2018 to 1/7/2019. Statistical analysis was performed in Microsoft Excel 2016 and R 3.6.0 program.*

Results: *The mean age of patients was 69.46±6.80 (range 60-82) with stage IIIb (15.38%) or IV (84.62%). Gemcitabine plus Carboplatin was the most common regimen (46.15%), followed by Vinorelbine (30.77%), Paclitaxel plus Carboplatin (19.23%) and Gemcitabine (3.85%). Chemotherapy-induced anemia was most frequent hematologic toxicity, up to grade 3. There was a significant difference in toxicity among the three toxicity risk groups (p=0.0019). The median time to progression was 5 months.*

Conclusion: *In elderly patients, the characteristics of our cohort was relatively identical to other studies in Vietnam. The median of PFS was 5 months in our sample. CARG score can be used to predict chemotoxicity before treating elderly patients.*

Keywords*: advanced non-small cell lung cancer, chemotoxicity*

I. INTRODUCTION

Lung cancer is the most common cancer and the leading cause of death worldwide according to Globocan [1]. This makes lung cancer a global burden. The primary lung cancer is divided into two groups: Non-small cell lung cancer (NSCLC) and Small-cell lung cancer (SCLC). NSCLC is the predominant type accounts for 85-90% of cases. And the prevalence of NSCLC is increasing steadily in the last two decades [2].

Nowadays, the number of elderly patients with lung cancer has been increasing. For instance, the mean age of lung cancer was 71 (range 31-95) in the UK [3] or 61.94±9.98 in the US [4]. In Vietnam, mean age at diagnosis was also greater than 60, and often diagnosed with advanced stage [5], [6].

Due to the impairment of the function of multiple

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organs, the chemotherapy-related toxicity become frequent in elderly patients. To minimize the toxicity, several mono chemotherapies are recommended as first-line for advanced NSCLC patients who age 70 or more [7]. In addition, several tools to predict chemotoxicity before indicating chemotherapy for elderly patients were published [8]. One of those was CARG tool, published on Cancer and Aging Research Group [9], can be used to predict the risk of chemotoxicity. Because of lacking needed data about predicting chemotoxicity and the outcome of elderly patients with advanced NSCLC in Vietnam, especially in Hue, we conducted this study with the aims:

- To describe clinical, subclinical features and treatment of advanced NSCLC in elderly patients.
- To evaluate the ability of predicting chemotherapy-related toxicity of CARG tool.
- To evaluate the efficacy of the treatment by the Progression-Free Survival (PFS).

II. PATIENTS & METHOD

A retrospective study was conducted in a cohort of 26 patients older than 60, diagnosed with advanced NSCLC and treated at least 3 cycles of chemotherapy at Hue University Hospital from 1/7/2018 to 1/7/2019. Data was collected from medical records and patient interview. We used CARG toxicity tool to subgroup sample into three risk strata (low, medium & high risk). Hematologic toxicities were captured by using the American Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE), version 3.0[10]. The proportions of toxicity in three risk strata were tested at the statistical significance level of 0.01. Time of progression disease were confirmed by applying the Response Evaluation Criteria in Solid Tumors (RECIST 1.1)[11]. The PFS was calculated by using Kaplan-Meier method.Statistical analysis was performed in Microsoft Excel 2016 and R 3.6.0 program.

III. RESULTS

3.1. Description of the cohort

Table 1. Patient characteristics (N=26)

Characteristics	No. of atients	% patients	Characteristics	No. of patients	% patients
Age, years			***Pathology***		
[60,65]	10	38.46	SCC	11	42.31
(65,70]	4	15.38	AC	8	30.77
(70,75]	7	26.92	ASC	1	3.85
(75,80]	3	11.54	Cytology	6	23.08
(80,85]	2	7.69	***Stage***		
Gender			IIIB	4	15.38
Male	14	53.85	IV	22	84.62
Female	12	46.15	***Treatment***		
Occupation			Monochemotherapy	9	34.62
Incapacity	20	76.92	Vino	8	30.77
Farmer	3	7.69	Gem	1	3.85
Other	3	7.69	Polychemotherapy	17	65.38
Chief complaint			Gem + Car	12	46.15
Cough	17	65.38	Pac + Car	5	19.23
Chest pain	9	34.62			
Dyspnea	4	15.38			
Adenopathy	1	3.84			
Others	4	15.38			
Smoking	16	61.54			
Mean of pack years:	28				

Abbreviation: *SCC - Squamous cell carcinoma; AC - Adenocarcinoma; ASC - Adenosquamous cell carcinoma; Vino - Vinorelbine; Gem - Gemcitabine; Car - Carboplatin; Pac - Paclitaxel*

The mean age of patients was 69.46±6.80 (range 60-82). The proportion male/female was approximately 1:1. Cough was the most frequent symptoms at admission (65.38%). Squamous cell carcinoma and Adenocarcinoma were the predominant histology types, accounting for 42.31% and 30.77% respectively. Patients were at stage IIIB (15.38%) and IV (84.62%). More than sixty-five percent of patients was treated with polychemotherapy, and of all cases, Gemcitabine plus Carboplatin was the most common regimen (36.84%), followed by Vinorelbine (30.77%), Paclitaxel plus Carboplatin (19.23%) and Gemcitabine (3.85%) (Table 1).

3.2. Comparison between CARG and Hematology toxicity

Table 2. Chemotherapy-related hematologic toxicity

Toxicity type	Grade 1		Grade 2		Grade 3		Grade 4 - 5	
	N	%	N	%	N	%	N	%
Hemoglobin	3	11.54	4	15.38	1	3.85	0	0.00
WBC	0	0.00	0	0.00	0	0.00	0	0.00
Platelets	1	3.85	0	0.00	0	0.00	0	0.00
***Abbreviation**: WBC - White blood cell*								

The hemoglobin toxicity was the most common chemotherapy-related hematologic toxicity (30.77%), up to grade 3 (Table 2).

Table 3. Ability of CARG to predict chemotherapy toxicity

Risk strata	No toxicity		Toxicity		Total (N)	P
	N	%	N	%		
0-5 (Low risk)	13	50.00	1	3.85	14	
6-9 (Medium)	4	15.38	6	23.08	10	0.0019
10-19(High risk)	0	0.00	2	7.08	2	

The cohort was divided into three strata based on the CARG score: Low risk (0-5) (N=14); Medium risk (6-9) (N=10); and High risk (10-19) (N=2). There was a significant difference in toxicity among the three toxicity risk groups (p=0.0019; table 3).

3.3. The outcome of the treatment

The general time to the failure of first-line (PFS) of 26 patients was showed in figure 2. The median of PFS was 5 months.

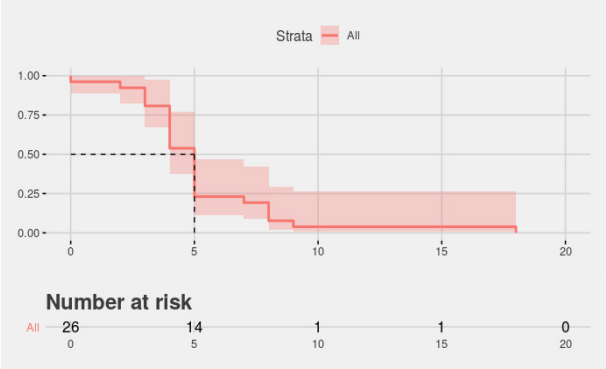

Figure 2. Progression Free Survival of treatment. The x axis is the time in months, the y axis is the survival probability.

IV. DISCUSSION

In the main clinicopathological characteristics: mean age at diagnosis was 69.46±6.80 (range 60-82), this is higher than the study of Nguyen Quang Trung (2018) at Nghe An oncology hospital (mean age: 63.8±10.6) because our study only selected elderly patients. The most common symptoms at admission were cough (65.38%) and chest pain (34.62%). These common symptoms are similar to the study of Hoang Dinh Cau et al, year but the proportions are different. His study described 389 patients who presented with cough at 26.47% and

chest pain at 36.50%. This difference may come from inclusion criteria that we focused on the elderly and also due to our small number of patients.

Our most common types of histology were squamous cell and adenocarcinoma as known in literature. We did have 6 patients diagnosed by cytology due to the general status and patients' refuse to reconfirm histology. This may modify the proportion of histologic type in our study and it is a problem in diagnosing older patients with lung cancer.

Patients were at stage IIIB (15.38%) and stage IV (84.62%). Patients were mainly treated by the regimen of Gemcitabine combined with carboplatin (46.15%), and vinorelbine 30.77%. These regimens were easy to admister and better tolerated hence the application for the elderly is feasible.

In our study, we emphasized on the application of CARG score to predict the toxicity prior to chemotherapy. We chose Fisher's Exact test to evaluate the difference between the proportion of toxicity in each group. The P-value less than 0.01 was statistically significant. This is identical to the study of Xiaomeng Nie in China, 2013 [12]. The drawback of our study was a small sample (N=26). We suggested collecting more data in order to apply the Chi-squared instead of Fisher's Exact test for enhancing the power of the hypothesis test.

Due to following up time of the cohort was not long enough so that we could not analyze the overall survival. We used DFS to evaluate the outcome of the treatment. The median time to progression of our cohort was 5 months. It is quite similar to other worldwide studies (5.4 months and 4 months in the study of Risteski 2013 [13] and Sweeney 2001 [14]). More observations and time of following up to analyze the difference between subgroups of regimens are needed. We are continueing follow up the cohort with aim of better characterizing the features of NSCLC at elderly, scoring the overall survival.

V. CONCLUSION

In general, the mean age of patients in our study was 69.46±6.80. The most common histology types were squamous cell carcinoma and adenocarcinoma. Patients were at stage IIIB and IV. Patients were mainly treated by the regimen of Gemcitabine combined with carboplatin (46.15%), and vinorelbine 30.77%. The median time to progression was 5 months in our cohort. CARG score can be applied in clinical settings to predict chemotoxicity before treating elderly patients.

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