Prognostic nomogram on clinicopathologic features and serum indicators for advanced non-small cell lung cancer patients treated with anti-PD-1 inhibitors

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Background: Immune checkpoint inhibitors (ICIs) have appeared as a promising therapy regimen for non-small cell lung cancer (NSCLC), but with an unsatisfying therapeutic response and inefficiency of a single predictive biomarker in patients' selection.

Methods: Central data of clinicopathologic features, peripheral blood indicators, and treatment records were collected in advanced NSCLC patients accepting PD-1 inhibitors in Changhai Hospital from July 2016 to September 2019. The OS probability nomogram was developed according to Akaike Information Criterion (stepAIC) selected factors. The predictive accuracy of the nomogram was assessed by discrimination and calibration. C-index and decision curve analysis were used to compare with the previously reported model (Botticelli Model). Computers resampling 500 times (Bootstrap 500 times) were performed to validate the model internally. According to the nomogram-based total point scores (TPS), we divided patients into different risk groups.

Results: A total of 110 patients were enrolled in this study. Six predictors, including liver metastasis, Eastern Cooperative Oncology Group Performance Status (ECOG PS), second- or third-line immunotherapy, baseline levels of CRP, cytokeratin 19 fragment (CYFRA21-1), were selected to set up the nomogram. The C-index of the current nomogram was 0.81 (95% CI: 0.72–0.80), keeping the same accuracy as the earlier one. Calibration plots showed slight underestimation in patients with predictive mortality <44% at 12 months and overestimation in patients with predictive mortality >44%. Decision curve analysis showed that the current nomogram was with a higher net benefit rate than the earlier model. According to the cut-off points of TPS, patients were divided into three subgroups: low risk (TPS ≤118), intermediate-risk (118< TPS ≤189), and high risk (TPS >189). A significant OS difference was observed among subgroups. Median OS was 6.6, 4.5, 1.3 months, respectively.

Conclusions: We proposed a novel nomogram model on easily available and inexpensive clinicopathologic features, peripheral blood indicators which is beneficial in individual risk assessment for advanced NSCLC patients before receiving PD-1 inhibitors, and assisting clinicians in accurately determining therapeutic decisions.

Keywords: Nomogram; immunotherapy; clinicopathologic characteristics; peripheral blood biomarkers; advanced non-small cell lung cancer (advanced NSCLC)

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Introduction

The latest epidemiological data indicate that lung cancer still links to the second most common cancer with the highest mortality rate on a global scale (1). As a malignant tumor with complex histological types, about 85% of lung cancer cases belong to non-small cell lung cancer cells (NSCLC) with a five-year survival rate of 19% (2,3).

In the past two decades, significant evolvement of treatment in NSCLC has been made with the introduction of several lines of small molecule tyrosine inhibitors in patients with EGFR, ALK, ROS1 mutations and the discovery of potent KRAS locking inhibitors. Similarly, with an impressive clinical benefit and tolerable adverse effect, immune checkpoint inhibitors (ICIs) have revolutionized the management of advanced NSCLC patients without actionable oncogenic drivers, improving the five-year survival rate to 16% (4). The fast-growing number of immunotherapeutic patients and undesirable response rates underline the importance of finding predictive biomarkers to aid clinical decision making. Widely tested as the expression of the PD-L1 on tumor cells or immune cells determined by immunohistochemistry has, PD-L1 is a suboptimal predictive biomarker due to the dynamic changes of PD-L1 expression over time, intra-tumoral heterogeneity, absence of a uniform guideline for test method and positive clinical threshold (5-7). Another extensively studied predictive biomarker tumor mutation burden (TMB) reflects the expression level of unstable genome induced neoantigens (8), which is promising in clinical application but with the limitation of high cost and shortage of consensus on detection methods (9,10). Other potential predictors such as tumor-infiltrating lymphocytes (11), tumor-specific genomics (12), were explored but have not yet been proven to be feasible in clinical practice.

Based on the multifactorial nature of cancer-immune interactions and ever-changing tumor immune microenvironment (TME), combining parameters are supposed to be the future of response prediction to immunotherapies. Blank (13) proposed a conception of "cancer immunogram" that enhanced T cell activity was the mechanism of the ultimate effect of immunotherapies. Seven dimensions may be the first framework of the "cancer immunogram." Using relevant parameters to set up a prognostic model may be an essential direction for the supervision of immunotherapeutic effects in patients with advanced NSCLC. Botticelli (14) developed a nomogram based on three clinicopathological factors, including liver and lung metastases and Eastern Cooperative Oncology Group Performance Status (ECOG PS), to predict overall survival (OS) probability in NSCLC patients accepting nivolumab.

Before, it was easily available, inexpensive, and allowing longitudinal observation that promoted to the increasing research of peripheral biomarkers such as neutrophil-to-Lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR) (15), serum tumor markers (16) and inflammatory parameters (17). The study aimed to develop an OS probability predictive model to evaluate individual risk in advanced NSCLC patients before receiving PD-1 inhibitors by using easily accessible clinicopathological parameters and serum biomarkers. We present the following article in accordance with the TRIPOD reporting checklist (available at http://dx.doi.org/10.21037/atm-20-4297).

Methods

Patients

We reviewed the electronic medical records of all patients with recurrent or advanced (stage IIIB to IV) NSCLC who had accepted PD-1 inhibitors (nivolumab or pembrolizumab) monotherapy or combined-therapy as first-line, maintenance, second-line, or further line regimen at Changhai Hospital between July 2016 and September 2019. From this review, we found a total of 126 patients receiving the injection of PD-1 inhibitors. Patients who received injection of PD-1 inhibitor with complete clinical data, therapeutic and following-up information were enrolled into data analysis. Patients with autoimmune diseases, other malignancies, and symptomatic interstitial lung diseases were excluded. According to the criteria, 110 individuals were included in data analysis. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013), and was reviewed and approved by the ethics committee of Changhai Hospital. All patients had signed informed consent.

Data acquisition

Data on clinicopathological features, peripheral blood indicators, and treatment records were extracted from the electronic inpatient record system or acquired by telephone. Follow-up, including gender, age, ECOG PS, smoking status, maximum lesion diameter, metastatic sites, EGFR/ALK/ROS1 mutation status, tumor staging, PD-L1 expression level, and other clinical pathological features were gathered. The baseline complete blood cell count

and its ratio, lactate dehydrogenase (LDH), C-reactive protein (CRP), albumin, carcinoembryonic antigen (CEA), cytokeratin 19 fragment (CYFRA21-1) and other serum indicators; immunotherapeutic regimens, commencement time of PD-1 inhibitors.

All data were last updated in December 2019. Complete blood count (CBC) was performed before the first injection of PD-1 inhibitor (baseline) and at the follow-up time point. Serum CRP concentration was determined with immunoturbidimetry. By immunoradiometric assay, CYFRA21-1 was measured. All operations and tests are carried out in accordance with the kit guidelines. Calculate formula: nutritional prognosis index (PNI) = albumin (g/L) + 5 × lymphocyte counts ×10^9/L; NLR = ANC/ALC; PLR = PLT/ALC; monocytes-to-lymphocyte ratio (MLR) = AMC/ALC. ANC, ALC, PLT and AMC were the counts of absolute neutrophils, absolute lymphocytes, platelet and monocytes, respectively.

Treatment and efficiency assessment

For the reason of the respective study, not all patients received standard injection does of nivolumab (3 mg/kg every 2 weeks) or pembrolizumab (200 mg every 3 weeks). Part of patients adopted combined therapy with antiangiogenic medicines, radiotherapy, or chemotherapies. Chest CT was undergone at every 8–9 weeks to evaluate the radiological response of tumors. The best response pattern and disease progression were evaluated according to the RESIST1.1. The definition of progression-free survival (PFS) and OS were following earlier reports. Patients without observed clinical or radiographic disease progression or who were still alive were censored on the date of the last follow-up.

Statistical analysis

Mean standard deviation or median (min-max) was used to describe continual variables. Categorical variables were presented as percentages. COX univariate and multivariate survival analysis were applied to evaluate the impact of peripheral blood parameters and clinicopathological factors on PFS and OS. Then, in univariate analysis, OS-related variables (P<0.05) were included in Stepwise Akaike Information Criterion (stepAIC) analysis to select out factors for the establishment of an OS probability predictive nomogram. C-index of discrimination and calibration curves were presented to qualify the predictive accuracy of

the nomogram (18). And 500 bootstrap re-samplings were performed to validate this model (19). C-index and decision curve analysis (DCA) was executed to compare the predictive accuracy and net benefit rates between the current model and the Botticelli model (14). At last, X-tile software was applied to determine the cut-off points of the nomogram-based total point scores (TPS). Kaplan-Meier curves and Log-rank tests were used to qualify the performance of current model in stratifying the risk of patients.

All statistical analyses were performed through the Empower Stats (http://www.empowerstats.com, X&Y Solutions, Inc., Boston, MA, USA) and R software 3.6.2 (http://www.r-project.org). A two-tailed P value of <0.05 was considered statistically significant.

Results

Patient characteristics

The average age of patients was 63.8±9.7 years, and 80.0% were males. Former or current smokers make up 63.6% of the subjects. Half of the patients were lung squamous carcinoma, forty-nine cases with adenocarcinoma, six cases with large cell carcinoma, or mixed adenosquamous cancer. Eighty-nine (80.9%) patients had ECOG PS 0 or 1, and 11.8% involved liver metastasis. There were 39 (35.5%), 24 (21.8%), and 47 (42.7%) patients received immunotherapy as first-line, second-line, or ≥ three-line treatment, respectively. Sixty-nine patients accepted PD-1 inhibitor combining with radiotherapy, antiangiogenic drugs or chemotherapy, and mono-immunotherapy was applied in 41 patients. Other baseline clinicopathological factors were shown in *Table 1*.

Patients had an average baseline level of CRP 19.1 mg/L and CYFRA21-1 6.5 ng/mL. Other baseline levels of serum parameters were presented in *Table 2*. At the last date of follow-up, the median OS was 5.5 months, thirty-eight patients died.

Univariate and multivariate COX survival analysis of the OS

COX univariate analysis showed that baseline level of ANC, NLR, PLR, CRP, CEA, CYFRA21-1 and treatment line, ECOG PS and smoking were related to OS (P<0.05, *Table 3*). Then, multivariate analysis through stepwise univariate analysis indicated that smoking was an independent protective factor for OS (HR =0.11, 95% CI:

Page 4 of 10

Chai et al. Prognostic nomogram for immunotherapeutic NSCLC patients

Table 1 Patients clinicopathological characteristics (n=110)

Variables	N (%)
Age (years)	63.8±9.7
Gender	
Male	88 (80.0)
Female	22 (20.0)
Smoking	
No	40 (36.4)
Yes	70 (63.6)
TNM stage	
III	25 (22.7)
IV	85 (77.3)
Pleural metastasis	
No	75 (68.2)
Yes	35 (31.8)
Lung metastasis	
No	59 (53.6)
Yes	51 (46.4)
Bone metastasis	
No	76 (69.1)
Yes	34 (30.9)
Liver metastasis	
No	97 (88.2)
Yes	13 (11.8)
Braine metastasis	
No	96 (87.3)
Yes	14 (12.7)
Histological types	
Squamous cell carcinoma	55 (50.0)
Adenocarcinoma	49 (44.5)
Other	6 (5.5)
EGFR mutation	
No	100 (90.9)
Yes	10 (9.1)
ROS1 mutation	
No	108 (98.2)
Yes	2 (1.8)

Table 1 (continued)

Table 1 (continued)

Variables	N (%)
ECOG PS	
0 or 1	89 (80.9)
2	21 (19.1)
Treatment line	
First-line	39 (35.5)
Second-line	24 (21.8)
≥ Three-line	47 (42.7)
Mono-immunotherapy	
No	69 (62.7)
Yes	41 (37.3)

Table 2 Baseline level of peripheral parameters

Parameters	Mean ± SD/median (Q1–Q3)
ANC ($\times 10^9$/L)	5.1±2.7
AMC ($\times 10^9$/L)	0.7±0.5
ALC ($\times 10^9$/L)	1.4±0.5
NLR	4.2±3.0
MLR	0.6±0.5
PLT ($\times 10^{12}$/L)	269.1±131.4
PLR	217±138
Hb (g/dL)	123±20
CRP (mg/L)	19.1 (1.2–250.0)
CEA (ng/mL)	4.7 (1.1–1,500.0)
CYFRA21-1 (ng/mL)	6.5 (0.6–100.0)
LDH (IU/L)	217.8±87.0
PNI	44.1±6.3
Alb (g/L)	37.6±4.3

NLR, neutrophil-to-lymphocyte ratio; MLR, monocytes-to-lymphocyte ratio; CRP, C-reactive protein; CEA, carcinoembryonic antigen; CYFRA21-1, cytokeratin 19 fragment; LDH, lactate dehydrogenase; PNI, nutritional prognosis index.

Table 3 Univariate and multivariate COX analysis for OS

Variables	Subgroup	Univariate analysis		Multivariate analysis	
		HR (95% CI)	P	HR (95% CI)	P
Gender	Female	1.4 (0.7–2.8)	0.389	–	–
Smoking	Yes	0.4 (0.2–0.8)	0.004	0.1 (0.0–0.3)	0.001
Pleural metastasis	Yes	1.8 (0.95–3.56)	0.071	–	–
Lung metastasis	Yes	0.96 (0.50–1.83)	0.898	–	–
Bone metastasis	Yes	1.72 (0.88–3.37)	0.111	–	–
Liver metastasis	Yes	2.80 (1.27–6.19)	0.011	–	–
Brain metastasis	Yes	0.95 (0.33–2.70)	0.924	–	–
Histological type	LUAD vs. LUSC	1.42 (0.72–2.80)	0.311	10.10 (2.17–47.01)	0.003
	Other vs. LUSC	1.02 (0.23–4.48)	0.975	–	–
EGFR	Yes	1.64 (0.63–4.25)	0.309	–	–
Age		1.03 (1.00–1.07)	0.082	–	–
ANC		1.15 (1.03–1.29)	0.012	–	–
CEA		1.00 (1.00–1.00)	0.005	–	–
CYFRA21-1		1.01 (1.00–1.02)	0.021	1.04 (1.01–1.06)	0.002
ALC		0.67 (0.33–1.34)	0.377	–	–
NLR		1.13 (1.05–1.21)	0.001	–	–
MLR		1.49 (1.02–2.18)	0.038	–	–
PLT		1.00 (1.00–1.00)	0.311	0.98 (0.97–1.00)	0.049
PLR		1.00 (1.00–1.00)	0.029	–	–
AEC		0.86 (0.26–2.81)	0.806	–	
Hb		0.98 (0.97–1.00)	0.041	0.95 (0.92–0.99)	0.007
CRP		1.01 (1.00–1.02)	0.001	1.02 (1.01–1.04)	0.007
LDH		1.00 (1.00–1.01)	0.289	–	–
PNI		0.97 (0.94–1.01)	0.207	–	–
Treatment line	2nd vs. 1st-line	2.64 (0.94–1.01)	0.078	19.75 (2.56–152.2)	0.004
	3rd vs. 1st-line	3.62 (1.37–9.60)	0.010	36.9 (5.11–266.56)	<0.001
ECOG	2 vs. ≤1	6.16 (3.12–12.16)	<0.001	–	–

OS, overall survival; NLR, neutrophil-to-lymphocyte ratio; MLR, monocytes-to-lymphocyte ratio; CRP, C-reactive protein; CEA, carcinoembryonic antigen; CYFRA21-1, cytokeratin 19 fragment; LDH, lactate dehydrogenase; PNI, nutritional prognosis index.

0.02–0.51, P=0.005), but baseline level of CRP (HR =1.02, 95% CI: 1.01–1.04, P=0.007), CYFRA21-1 (HR =1.04, 95% CI: 1.00–1.06, P=0.002), PLT (HR=0.98, 95% CI: 0.97–1.00, P=0.0493) and second-line treatment (HR =19.75, 95% CI: 2.56–152.22, P=0.004) or third-line treatment (HR =36.9, 95% CI: 5.11–266.56, P<0.001) were significantly

associated with shortened OS.

Establishment and validation of OS probability prediction nomogram

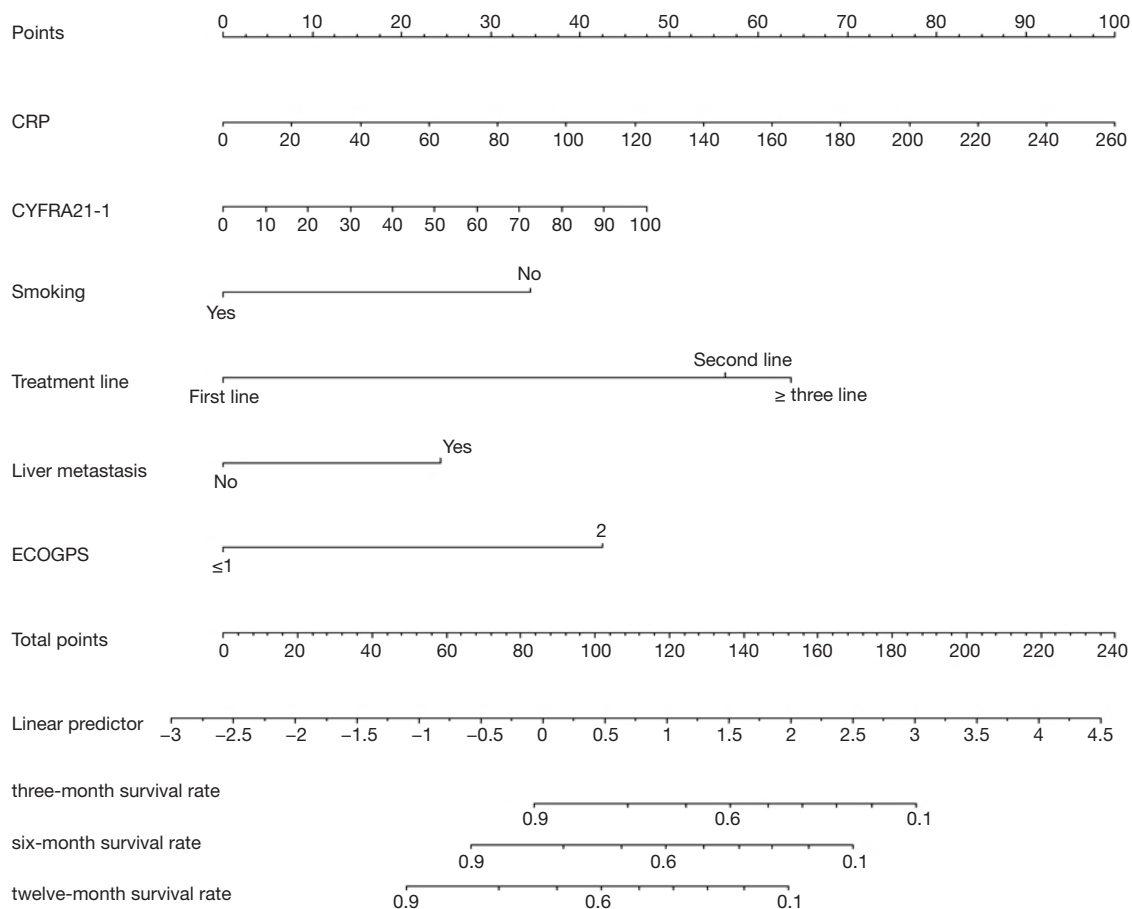In the COX univariate analysis, variables related to OS

Figure 1 Prognostic nomogram of OS probability at 3-, 6- and 12-month in advanced NSCLC patients treated with PD-1 inhibitors For each factor, the number of corresponding risk points can be determined by delineating a vertical line from the prognostic factor to the points raw (0 to 100), and sum the corresponding risk points to determine the total points for each patient. The corresponding probability of survival at 3, 6, and 12 months can be obtained by drawing a straight line from the total points axis to the OS probability axis. OS, overall survival; NSCLC, non-small cell lung cancer.

(P<0.05) were screened through stepwise AIC regression. Smoking, liver metastasis, treatment lines, ECOG PS, the baseline level of CYFRA21-1 and CRP were integrated into the dynamic prediction nomogram model to calculate survival probability at 3, 6, and 12 months in advanced NSCLC patients treated with PD-1 inhibitors (*Figure 1*).

Each prognostic parameter has a corresponding number of risk points, which can be obtained by delineating a vertical line from the prognostic factor to the points raw. Then, the corresponding risk points of each parameter were summed to determine the total points scored. Finally, from the total points axis, a vertical line can be drawn towards the OS probability axis to obtain the 3-, 6- and 12-month OS probability for a specific patient. For example, a smoking (0 point) patient with ECOG PS 1 (0 points), liver

metastasis (25 points), a baseline level of CRP 100 mg/L (39 points), CYFRA21-1 40 ng/L (15.5 points) and accepting PD-1 inhibitors as second-line therapy (58 points), the sum of the total risk points was 137.5 points. By drawing a vertical line down the "3-, 6- and 12-month survival probability" axis, the survival probability of 3-, 6- and 12-month was 58%, 40%, and 12%, respectively.

C-index for the current OS model was 0.81 (95% CI: 0.72–0.90), showed it had distinguished discrimination. According to the calibration curve (*Figure 2*), among patients with actual mortality of greater than 44%, the model would overestimate mortality risk. For example, some individuals in whom the model predicted mortality risk of 60% (actual mortality of approximately 50%) might improperly refuse immunotherapy due to the high estimated
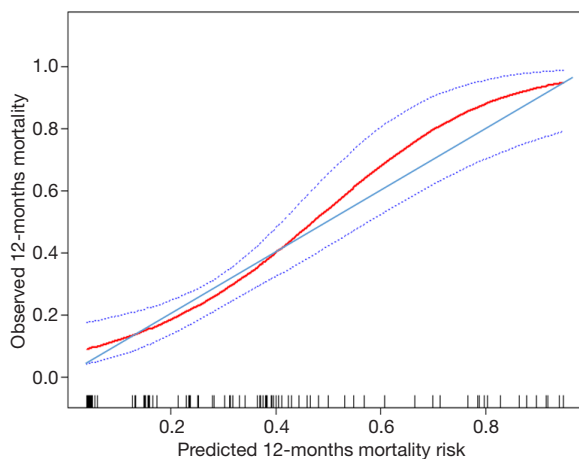

Figure 2 Calibration plot of predicted mortality-probability against the observed mortality-probability at 12 months. The red regression curve is plotted to demonstrate the general trend; the dashed curve shows the 95% CI of the calibration curve; the blue line shows the ideal calibration line.
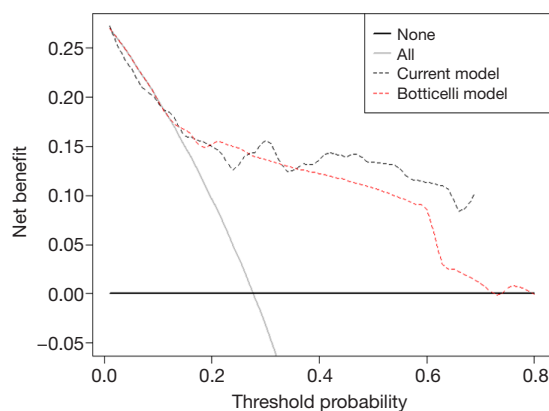

Figure 3 Decision curve analysis for 6-month survival black dotted line: current nomogram; red dotted line: Botticelli nomogram. Y-axis: net benefit = total benefits (true positives) – harms (false positives). The straight grey line represents the assumption that all patients will die at six months, and the black horizontal line represents the assumption that no patients will die at six months.

risk of death and low expectation of therapeutic benefit. However, among patients with actual mortality of lower than 44%, the model would underestimate mortality risk. For example, some individuals in whom the model predicted mortality risk of 30% (actual mortality of approximately 35%) might improperly accept immunotherapy due to the low estimated risk of death and high expectation of therapeutic benefit. Therefore, the current model had an
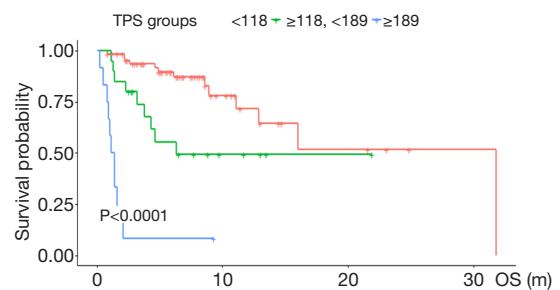

Figure 4 Kaplan-Meier curves for three subgroups based on the predictors from the nomogram. The red curve, green curve, and blue curve represent the group of TPS ≤118, 118< TPS ≤189, and TPS >189, respectively. The vertical axis is the survival rate, and the horizontal axis is over survival time (month). TPS, total point score.

adequate calibration ability, but using the model would lead some patients to refuse or accept immunotherapy, impairing benefits from that treatment inappropriately.

Comparison of current nomogram and reported nomogram

Comparison of the C-index of current nomogram model 0.81 (95% CI: 0.72–0.90) with the reported model (Botticelli model) 0.76 (95% CI: 0.68–0.81) presented no statistical difference indicating that the current model kept the same predictive accuracy as the Botticelli model. Decision curve analysis for 6-months survival (*Figure 3*) revealed that the current nomogram had a higher net benefit rate than the Botticelli nomogram, implying that patients could benefit from using the current model to guide clinical treatment decisions.

Performance of the nomogram in stratifying patient risk

Patients were divided into three subgroups according to the cut-off value of nomogram-based total score (TPS): low-risk (TPS ≤118, 65 cases), intermediate-risk (118< TPS ≤189, 20 cases), and high-risk (TPS >189, 12 cases). A significant OS difference was observed among subgroups. Median OS was 6.6, 4.5, 1.3 months, respectively. Kaplan-Meier survival curve analysis manifested that patients in the high-risk group were linked to a shortened OS (*Figure 4*).

Discussion

ICIs with significant treatment effects and tolerable adverse events had developed a new standard management pattern for NSCLC patients. And there is an urgent need

Page 8 of 10

Chai et al. Prognostic nomogram for immunotherapeutic NSCLC patients

for predictive markers to precisely select immunotherapy optimal individuals. In the study, we used the easily accessible clinicopathological characteristics and serum parameters to establish a survival prognostic nomogram model for advanced NSCLC patients treated with PD-1 inhibitors. The nomogram model with superb predictive accuracy and discriminative ability could be applied to estimate individual risk for advanced NSCLC patients before the commencement of immunotherapy and assist in the decision-making process in clinical practice.

The establishing indicators between the current and reported models (14) were diverse for the different factors screening methods. Another reason was that our study included peripheral biomarkers. Comparison of the C-index between current nomogram (C-index 0.81, 95% CI: 0.72–0.90) and reported nomogram (C-index 0.76, 95% CI: 0.65–0.85) implied that the predictive accuracy of current model kept the similar accuracy to reported model. Nevertheless, the current model was based on the real-world data of advanced NSCLC patients who received diversely immunotherapeutic strategies. The reported model was based on data of advanced NSCLC patients who received nivolumab as second-line therapy. The current nomogram might have a larger applicable population. Additionally, decision curve analysis for 6-month survival revealed a higher net benefit rate of the current model than reported one.

As a classic indicator for patient behavioral status, clinical trials and real-world studies all had demonstrated that ECOG PS ≥2 was an independent predictor for dismal prognosis in NSCLC patients accepting systemic therapies (20,21). Hence, the ECOG PS score needs to be routinely assessed in the clinical decision-making process. Studies reported that receiving Pembrolizumab combined with platinum-based chemotherapy as a first-line regimen was the optimal management for advanced NSCLC patients, and with the backward-shift of treatment lines benefit from immunotherapy would be impaired (22,23). Our study also showed that the backward shift of treatment lines was paralleled to an increased prognostic risk score indicating the moment of adopting ICIs might impact clinical outcomes.

COX univariate and multivariate survival analysis manifested that tobacco exposure history was an independent protective factor for NSCLC patients adopting ICIs. The potential mechanism was that tobacco carcinogen-related mutagenesis was linked to elevated nonsynonymous mutation burden promoting the expression of neoantigens, which makes tumor cells more immunogenic, improving the recognition ability and sensitivity of T cells (24). Another

possible mechanism was that tobacco exposure could shape chronic inflammation microenvironment to recruit tumor-infiltrating lymphocytes (TILs) and release interferon-γ (IFN-γ) inducing PD-L1 expression and enhancing the stability of the PD-L1. As a routinely examined clinical marker, elevated serum level of CRP could reflect the host's chronic inflammatory status, and immune response to the tumor. In the study, baseline CRP level was positively correlated with patients' risk scores. CRP could be through IL-6/JAK/STAT3 signal pathway to promote cancer immune evasion (25).

Previous data demonstrated that NSCLC patients with liver metastasis had a reduced 3-year survival rate, inadequate treatment response, and shortened PFS in immunotherapy (26), and our study had observed the same association. Incomplete activation of CD8+T cells, capturing and clear of activated CD8+T cells could induce liver-related peripheral immune tolerance (27). Also, Bamboat (28) observed that difference in dendritic cell secretions in peripheral blood and liver was a potential interpretation of the diverse quantity and activity of cytotoxic T cells in the liver and circulation.

Serum tumor markers such as CEA and CYFRA 21-1 had been identified as useful prognostic and longitudinal monitoring biomarkers in NSCLC patients receiving chemotherapy (29) and targeted therapy (30). Recently, studies also found that serum level of CYFRA21-1 or CEA could assist in predicting immunotherapy efficacy (16). Our data showed that baseline levels of CEA and CYFRA21-1 were positively correlated with the patient's risk score before immunotherapy. CEA and CYFRA21-1 both are commonly used clinical indicators. The serum concentration of CYFRA21-1 is particularly elevated in the carcinoid tumors and LUSC (31). In this study, only CYFRA21-1 was selected as a predictive model construction factor, which may be related to the larger proportion of males and LUSC patients in this study.

Given the retrospective nature of the study, there were certain limitations. Firstly, as a retrospective study cannot exclude all potential biases. Secondly, many studies were inclined to transfer continuous parameters to binary variables, but we did not adopt the usual conversion. Moons (19) deemed that converting continuous variables into binary variables might lead to loss of major information and reduce the test power. Thirdly, only monocentric data of advanced NSCLC patients receiving PD-1 inhibitors were used to develop the nomogram with small sample sizes and imbalanced male-to-female ratio. Further larger scale,

multi-center prospective studies, and external validation should be performed to check whether these results were suitable for the general population. At last, this study only focused on the prognostic function of clinicopathological characteristics and routinely used serum parameters in NSCLC patients treated with PD-1 inhibitors. Other broadly explored predictors such as PD-L1 and TMB were not included in the analysis.

In conclusion, the nomogram based on easily accessible clinicopathological characteristics and serum parameters was a simple and inexpensive prognostic tool for advanced NSCLC patients treated with PD-1 inhibitors, which could be adopted in individual risk assessment before patients receiving PD-1 inhibitors as well as assisting clinicians in making optimal therapeutic decisions.

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Footnote

Reporting Checklist: The authors have completed the TRIPOD reporting checklist. Available at http://dx.doi.org/10.21037/atm-20-4297

Data Sharing Statement: Available at http://dx.doi.org/10.21037/atm-20-4297

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013), and was reviewed and approved by the ethics committee of Changhai Hospital. All patients had signed informed consent.

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