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INTRODUCTION

The development of immune checkpoint inhibitor therapy (ICI) offered advanced non-small cell lung cancer (NSCLC) patients a new highly effective therapy, but only a minority of patients respond. Prior small studies in highly-selected populations suggested that impaired pre-treatment nutrition & chronic inflammation were strongly associated with a poor response, likely related to impaired immune function.

We investigated this association in a large, diverse, real-world cohort of metastatic NSCLC patients to provide definitive documentation of this clinically important finding.

METHODS

Design:

- Harmonized Flatiron Health Research Database were collected from 280 diverse oncology U.S. practices from 2017-2024.
- Investigated the results of ICI treatment of metastatic NSCLC patients including progression-free survival (PFS) and overall survival (OS) rates.
- Compared relationship of PFS and OS rates to measures of their nutritional and inflammatory status.
- Descriptive analysis was performed with frequency and percentage for categorical variables and mean, standard deviation, and range for continuous variables.
- Progression-free survival (PFS) and overall survival (OS) were defined as time interval from the first date of immunotherapy treatment to date of disease progression and death, respectively.

DISCUSSION AND CONCLUSION

Actionable Take Away Message

- Using the large database population with balanced diversity in age, gender, race and geographic location of immunotherapy-treated metastatic NSCLC patients, **PFS and OS were strongly dependent on the pre-treatment nutrition and inflammatory state as documented by multiple different blood and clinical indicators.**

Future Direction for Research

- We recommend that advanced NSCLC patients with pre-treatment nutritional impairment with its concomitant chronic inflammation should be promptly referred for nutritional counseling and preferably a pre-habilitation program prior to starting ICI therapy.

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RESULTS

- 27,450** patients with advanced NSCLC received immunotherapy in the Flatiron real-world database.
- PFS** by univariate and multivariate analysis was significantly associated with measures of nutritional impairment and inflammation, Figure 1.
- The most dramatic association was depressed **OS** when there was compromised nutrition and chronic inflammation, such as with low serum albumin levels and a high Systemic Immune Inflammation Index, Table 1 and Figure 2.

Table 1. Overall Survival Based on Pre-Treatment Variables

Factor	Level / Median	Univariable				Multivariable			
		N	HR	95% CI	p value	N	HR	95% CI	p value
Birth sex	F	12843	1			2431	1		
	M	14396	1.198	1.165-1.231	<0.001	2700	1.215	1.137-1.298	<0.001
Race	AA	2963	1			588	1		
	Asian	514	0.837	0.742-0.944	0.004	90	1.172	0.891-1.542	0.257
	Other Race	2078	1.236	1.157-1.32	<0.001	434	1.290	1.118-1.489	<0.001
	White	18274	1.117	1.066-1.169	<0.001	4019	1.069	0.963-1.186	0.212
Smoking status	History of smoking	24693	1						
	No history of smoking	2525	0.951	0.906-0.998	0.041				
Histology	Non-squamous cell carcinoma	19066	1						
	NSCLC histology NOS	1122	1.222	1.141-1.31	<0.001				
	Squamous cell carcinoma	7051	1.227	1.189-1.266	<0.001				
PD-L1 tumor expression score	< 1%(Negative)	6367	1						
	1-49% (Low)	5854	0.863	0.829-0.9	<0.001				
	>50% (High)	5885	0.757	0.726-0.789	<0.001				
ECOG group	0	5692	1			1468	1		
	1	9830	1.323	1.272-1.376	<0.001	2518	1.231	1.138-1.331	<0.001
	2	3930	1.996	1.904-2.092	<0.001	956	1.674	1.52-1.844	<0.001
	3-4	980	2.746	2.548-2.96	<0.001	189	2.216	1.868-2.629	<0.001
Immunotherapy treatment line number	1	21522	1			3807			
	2	4809	1.142	1.101-1.184	<0.001	1109	1.11	1.024-1.205	0.012
	>=3	908	1.212	1.122-1.308	<0.001	215	1.265	1.071-1.494	0.006
Age at first immunotherapy start date			1.014	1.012-1.015	<0.001		1.009	1.006-1.013	<0.001
*Cholesterol	160.5	566	0.970	0.849-1.108	0.852				
*Albumin	38	21362	0.799	0.784-0.814	<0.001	5131	0.977	0.97-0.985	<0.001
*Lymphocytes	0.0792	21323	0.860	0.84-0.88	<0.001	5131	0.649	0.538-0.784	<0.001
*Monocytes	0.67	20729	1.137	1.112-1.162	<0.001	5131	1.165	1.058-1.282	0.002
*Neutrophils	6.17	19209	1.233	1.211-1.256	<0.001	5131	1.031	1.02-1.043	<0.001
*† Platelets	274	21136	1.113	1.087-1.14	<0.001	5131	1.001	1-1.001	<0.001
*Hemoglobin	12.2	23775	0.831	0.812-0.851	<0.001	5131	0.961	0.942-0.98	<0.001
*Leukocytes	8.5	21826	1.159	1.139-1.18	<0.001				
*† NLR	5.385	18797	1.205	1.184-1.226	<0.001	5131	1.03	1.02-1.039	<0.001
† ALI	174.272	15533	0.684	0.642-0.729	<0.001				
† SIRI	3.486	18153	1.129	1.115-1.143	<0.001				
† SII	1483.372	17732	1.164	1.146-1.183	<0.001	5131	0.999	0.999-0.999	<0.001
† LMR	1.789	20384	0.805	0.769-0.842	<0.001				
*PNI	38	19246	0.803	0.787-0.819	<0.001				
*GNRI	103.646	19819	0.815	0.795-0.835	<0.001	5131	0.996	0.993-0.999	0.014
*CONUT	1	471	1.162	0.995-1.358	0.058				
*3-months weight change pre-treatment (%)		17367	0.9	0.873-0.928	<0.001				
*6-months weight change pre-treatment (%)		18101	0.895	0.869-0.923	<0.001				
*12-months weight change pre-treatment (%)		18446	0.901	0.874-0.928	<0.001				

*Indicator of malnutrition; † Indicator of inflammation

Abbreviations: NLR=Neutrophil to lymphocyte ratio; ALI= Advance Lung Cancer Inflammation Index; SIRI= Systemic Immune Response Index; SII=Systemic Immune Inflammation Index; LMR=Lymphocyte to monocyte ratio; PNI=Prognostic Nutritional Index; GNRI= Geriatric Nutritional Risk Index; CONUT=Controlling Nutritional Status.

Figure 1. Progression Free Survival Multivariable Analysis Based on Pre-Treatment Variables

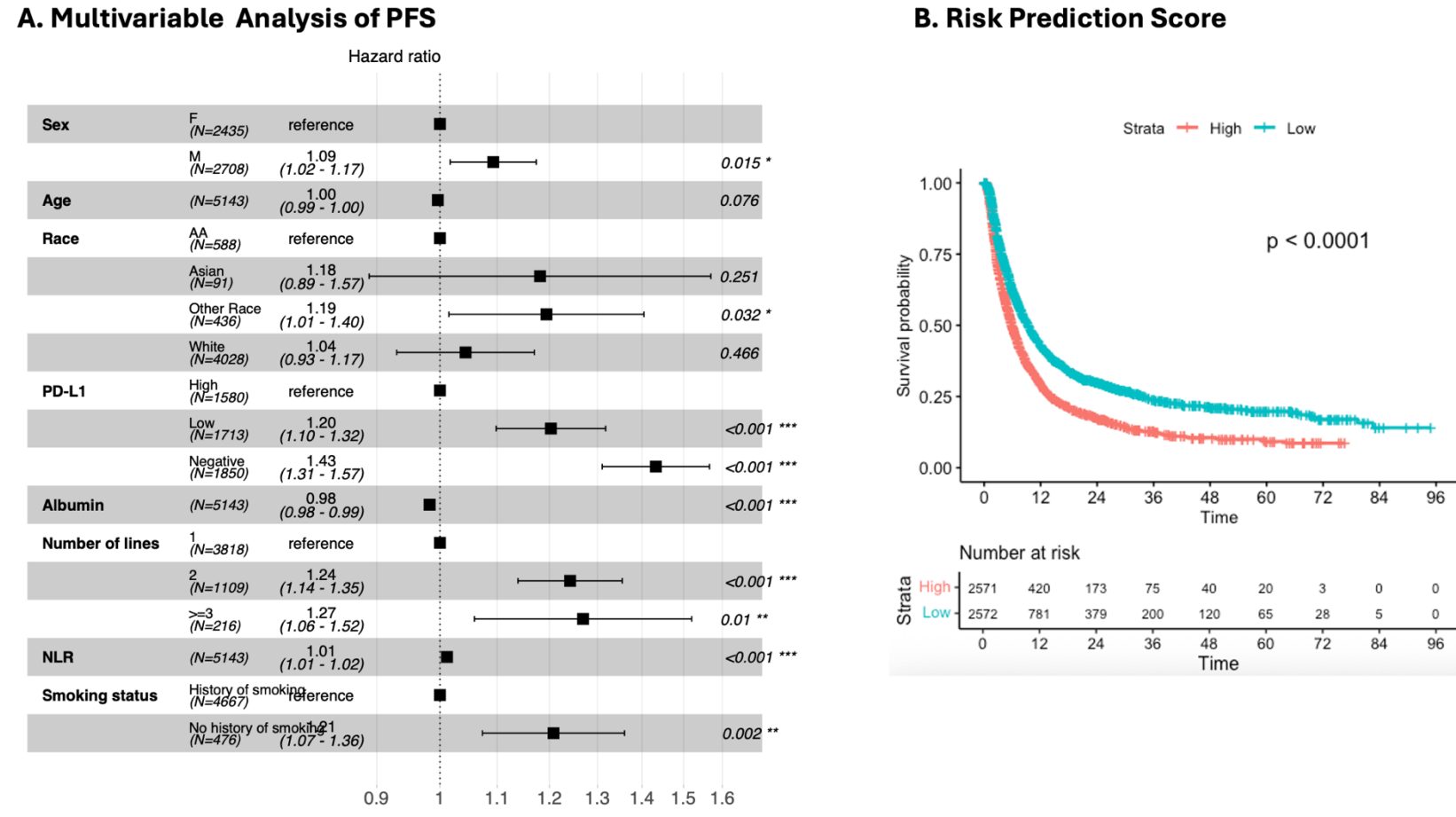
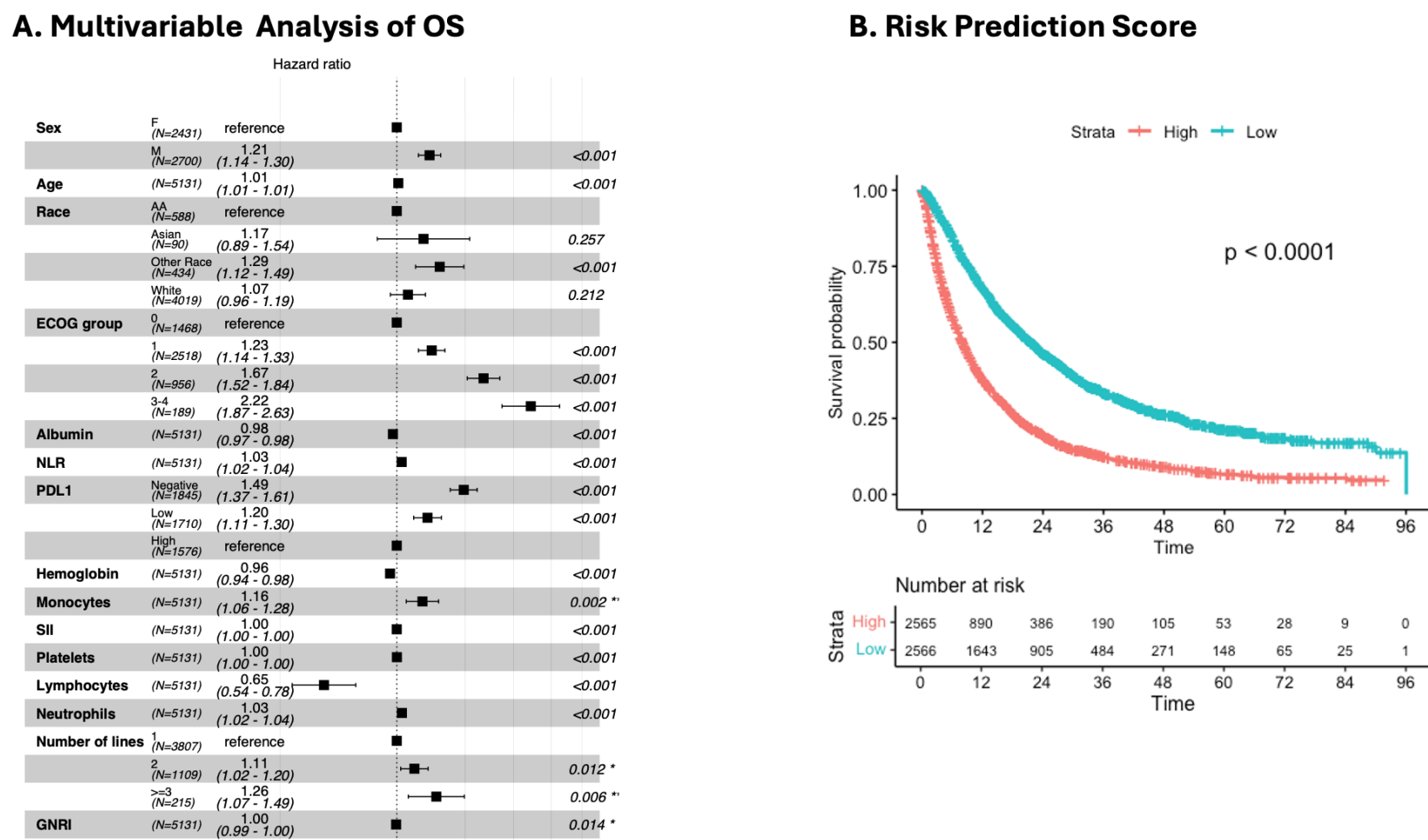


Figure 2. Overall Survival Based on Pre-Treatment Variables



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