Allostatic Load Markers as Predictors of Melanoma Outcomes

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Introduction

- **Melanoma**, while accounting for only about 1% of skin cancers, is responsible for **most skin cancer-related deaths** (Saginala et al., 2021).
- Immune checkpoint blockade (ICB) therapy has revolutionized the management of advanced melanoma.
- However, **not all patients respond to ICB therapy** and those who initially respond may develop resistance.
- In other cancer types (prostate, breast) **therapeutic response correlates to allostatic load** (AL).
- Allostatic load quantifies the wear and tear on the body due to **repeated adaptation to stressors**, encompassing metrics like blood pressure, cholesterol, and various hormonal measures (Guidi et al., 2021).
- Our study explores allostatic load and outcomes for advanced disease melanoma patients who received immunotherapy.

Methods

Patient Cohort and Data Extraction:

- Utilized Epic healthcare software for patient data extraction.
- Incorporated two pre-existing patient datasets
- Verified surgery and immunotherapy start dates for each subject via Epic's "Encounters", "Notes", and "Pathology" sections

Allostatic Load Data Retrieval:

- Extracted physiologic and laboratory markers as close in proximity to ICB start as possible.
  - *Physiological markers*: systolic blood pressure (SBP), diastolic blood pressure (DBP), heart rate (HR), and body mass index (BMI).
  - *Laboratory markers*: hemoglobin, albumin, creatinine, white blood count (WBC), eGFRNAA, alkaline phosphatase (Alk Phos), glucose, and blood urea nitrogen (BUN).
- Of the initial 141 subjects, 66 were included for analysis. Reasons for exclusion included mismatched demographics data, unavailability of pre-immunotherapy lab values and recurrence data.

Data Processing and Analysis Preparation:

- Assigned binary codes to each allostatic load marker based on established clinical cutoffs (e.g., SBP ≥140 was labeled "1", <140 was labeled "0"). See Table 1.

Methods Cont.

- Calculated cumulative allostatic load scores for each patient. Grouped patients into:
  - "Low Allostatic Load" (cumulative score 0 – 2).
  - "High Allostatic Load" (cumulative score 3 – 5).
- Constructed demographic table categorizing data by allostatic load levels, detailing Age, Sex, and BMI per category.
- Created Kaplan-Meier plots to represent the distribution of overall survival (OS) and progression-free survival (PFS) from the date of ICB start.
  - Patients who remained alive were censored at the last vital status date for OS. Patients who remained alive and progression-free were censored at the last clinic visit for PFS.

Table 1.

Thresholds for Allostatic Load Marker Coding

Allostatic Load Marker	0	1
SBP (mmHg)	<140	≥140
DBP (mmHg)	<90	≥90
HR (beats/min)	<100	≥100
BMI (kg/m^2)	<29.50	≥29.50
Hemoglobin (gm/dL)	12.0-16.0 (F)*, 14.0-18.0 (M)**	≤12 (F)*, ≤14 (M)**
Albumin (gm/dL)	>4.0	≤4.0
Creatinine (gm/dL)	<1.2 (F)*, <1.4 (M)**	≥1.2 (F)*, ≥1.4 (M)**
WBC (K/uL)	<11.0	≥11.0
EGRFNAA (mL/min/1.75 m^2)	>60	≤60
Alk Phos (U/L)	<147	≥147
Glucose (gm/dL)	<110	≥110
BUN (gm/dL)	<18	≥18

*Female
**Male

Results

Table 2: Demographics of All Patients

Group	Age (Mean)	Sex (M/F)	BMI (Mean)
0 – 2	62.14	29/14	25.56
3 – 5	69.94	14/8	26.38

Table 3: Summary of Progression-Free Survival: All Patients

Group	N	N Events	Median	Lower 95% CI	Upper 95% CI
0 – 2	41	15	3.45	2.67	N/A
3 – 5	22	9	N/A	2.42	N/A

Table 4: Estimates of Progression-Free Survival: All Patients: 1, 3, and 5 years

Group	Year	Progression-Free Survival	LCI	UCI
0 – 2	1	79.8%	68.2%	93.3%
0 – 2	3	61.2%	46.0%	81.3%
0 – 2	5	45.3%	27.2%	75.6%
3 – 5	1	67.4%	50.1%	90.5%
3 – 5	3	56.1%	38.1%	82.8%
3 – 5	5	56.1%	38.1%	82.8%

Results Cont.

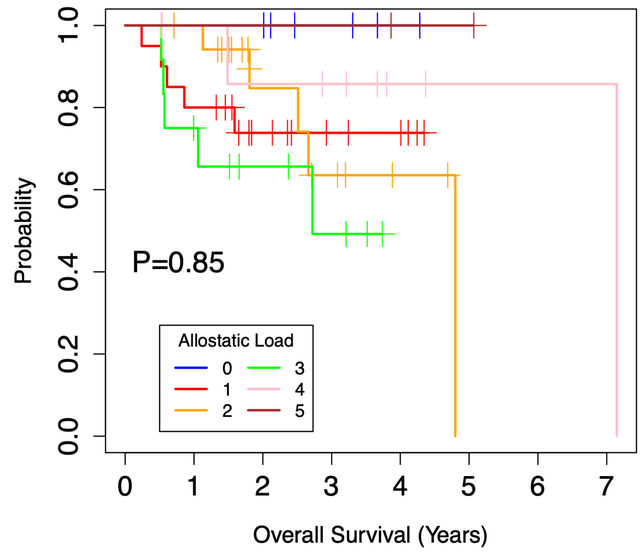

Fig. 1. Kaplan-Meier plot of PFS by allostatic load score. There is no evidence of a difference between the groups.

Table 5: Summary of Overall Survival: All Patients

Group	N	N Events	Median	Lower 95% CI	Upper 95% CI
0 – 2	44	10	4.80	N/A	N/A
3 – 5	23	7	7.15	N/A	N/A

Table 6: Estimates of Overall Survival: All Patients: 1, 3, and 5 years

Group	Year	Progression-Free Survival	LCI	UCI
0 – 2	1	90.9%	82.7%	99.8%
0 – 2	3	72.7%	57.9%	91.2%
0 – 2	5	0.0%	N/A	N/A
3 – 5	1	86.1%	72.6%	100%
3 – 5	3	69.6%	51.7%	93.7%
3 – 5	5	69.6%	51.7%	93.7%

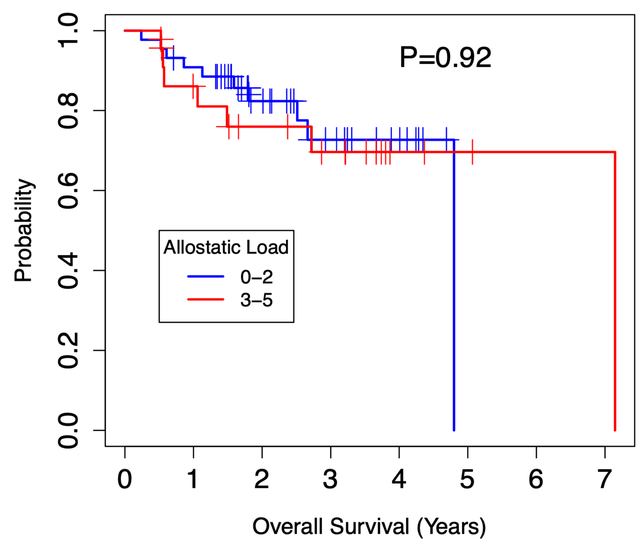

Fig. 2. Kaplan-Meier plot of OS by allostatic load score. There is no evidence of a difference between the groups.

Conclusions

After analyzing Kaplan-Meier curves, we found no correlation between allostatic load score and survival. Our analysis was limited to 66 of the original 141 patients, all from the late immunotherapy group, due to data challenges. This reduced sample size may have influenced our results.