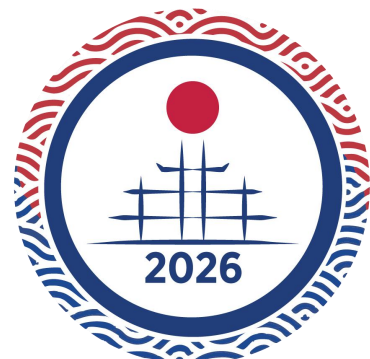




P3.301: Prognostic Impact of Non-Target Immune Organ Radiation Dose in ES-SCLC Treated with Radiotherapy and Chemoimmunotherapy

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1. Background

- Chemoimmunotherapy is the current first-line standard for ES-SCLC, but survival remains limited.
- LDRT may enhance antitumor immunity, yet substantial heterogeneity in outcomes persists.
- During thoracic irradiation, immune-relevant non-target organs involved in circulation and immune homeostasis also receive radiation exposure.
- We hypothesized that greater radiation exposure to these organs may contribute to post-RT immune changes and poorer survival.

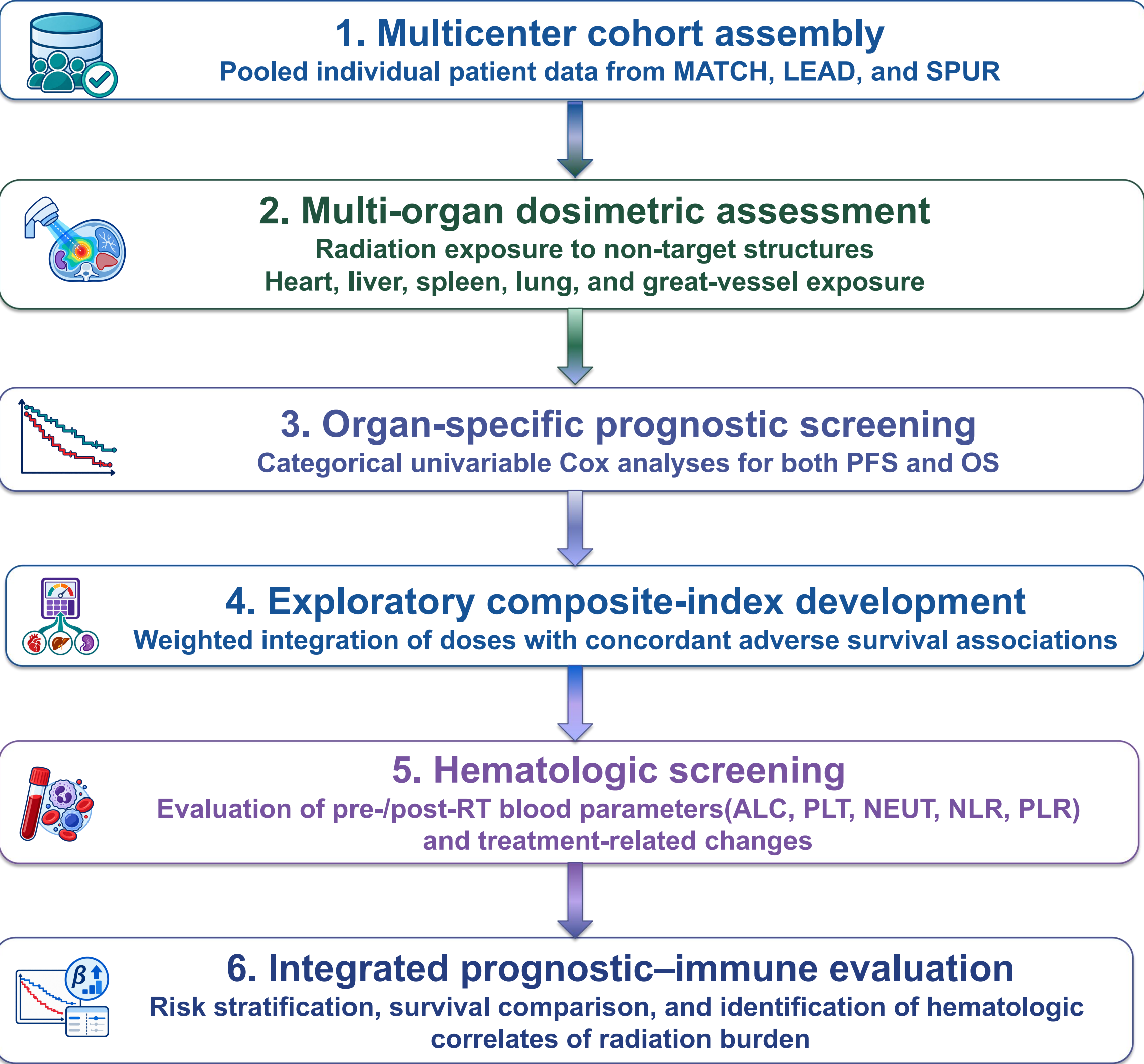
2. Objective

To evaluate the prognostic impact of non-target immune-organ radiation exposure and develop an exploratory multi-organ dose-burden index in ES-SCLC treated with LDRT plus chemoimmunotherapy.

3. Methods

Multicenter individual patient data from the prospective phase II MATCH, LEAD, and SPUR studies were pooled for analysis (N=88).

Study workflow



4. Results

(1) Organ-specific categorical Cox analyses

Same organ-specific cutoff applied to both PFS and OS

Organ	Cutoff	PFS_HR	PFS_P	OS_HR	OS_P
Heart	279.5 cGy	1.99	0.028	2.39	0.036
Liver	25 cGy	1.96	0.009	2.40	0.005
Spleen	4 cGy	1.86	0.047	2.67	0.027

All three organs showed concordant adverse associations with PFS and OS.

(2) Exploratory development of IODBI

Immune Organ Dose Burden Index (IODBI)

$$\text{IODBI} = 0.15 \times \text{Heart Dose} + 0.75 \times \text{Liver Dose} + 0.10 \times \text{Spleen Dose}$$

Cutoff: 93 cGy

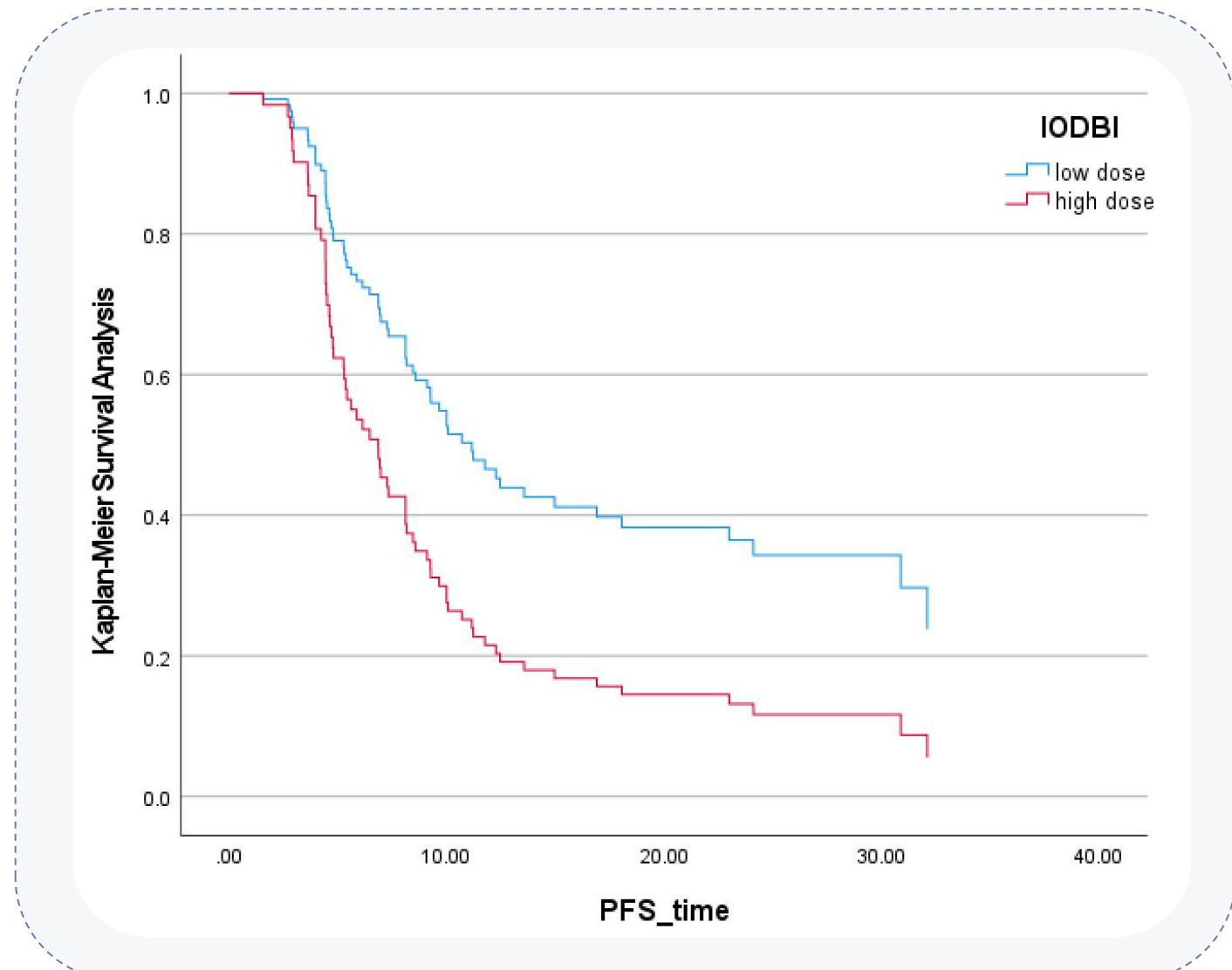
Low IODBI <93 cGy
n = 53 (60.2%)

High IODBI ≥93 cGy
n = 35 (39.8%)

Exploratory, data-driven index derived within the pooled cohort.

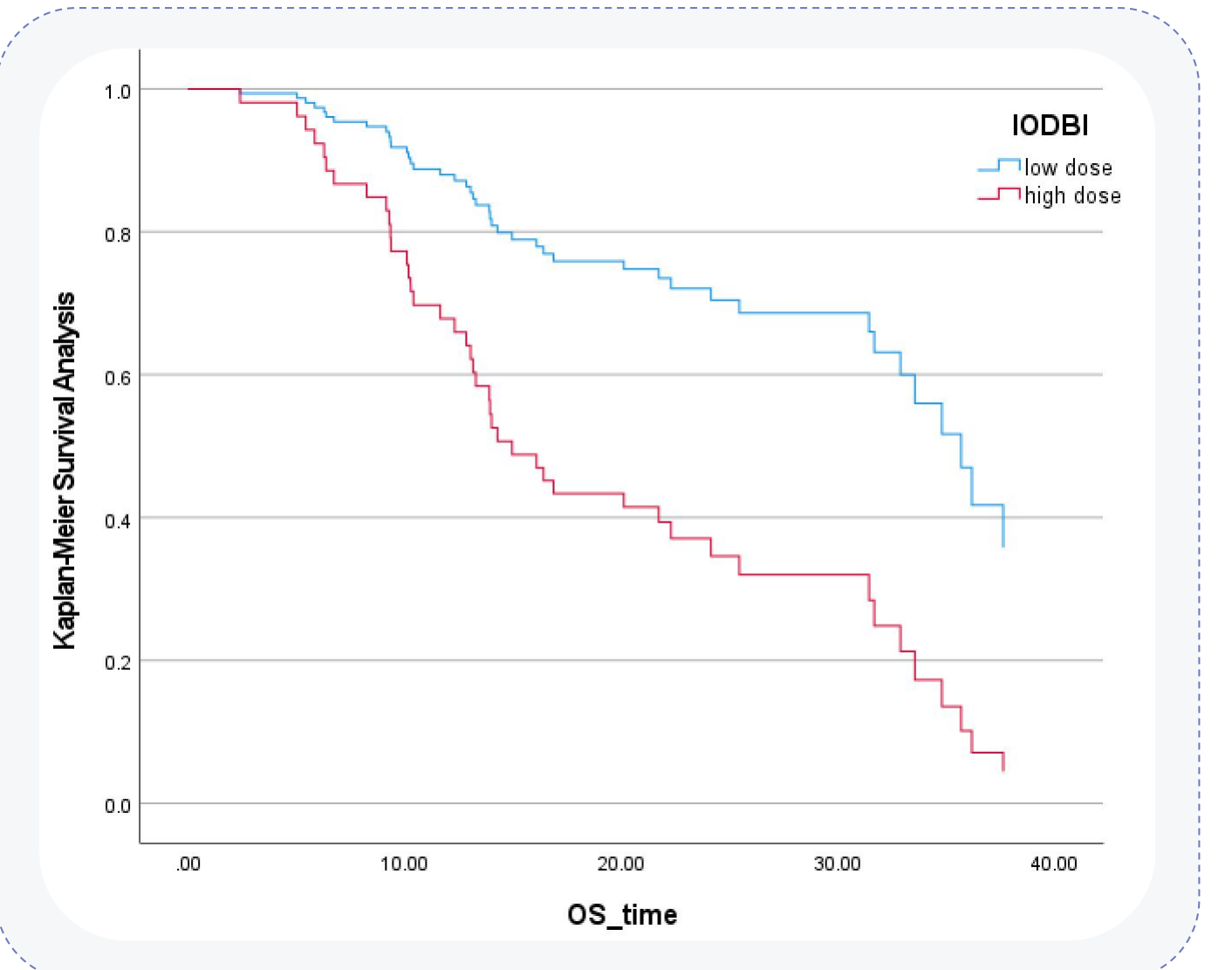
(3) Survival impact of IODBI

PFS
High vs Low IODBI
HR = 2.01
P = 0.006



~2-fold higher risk of progression

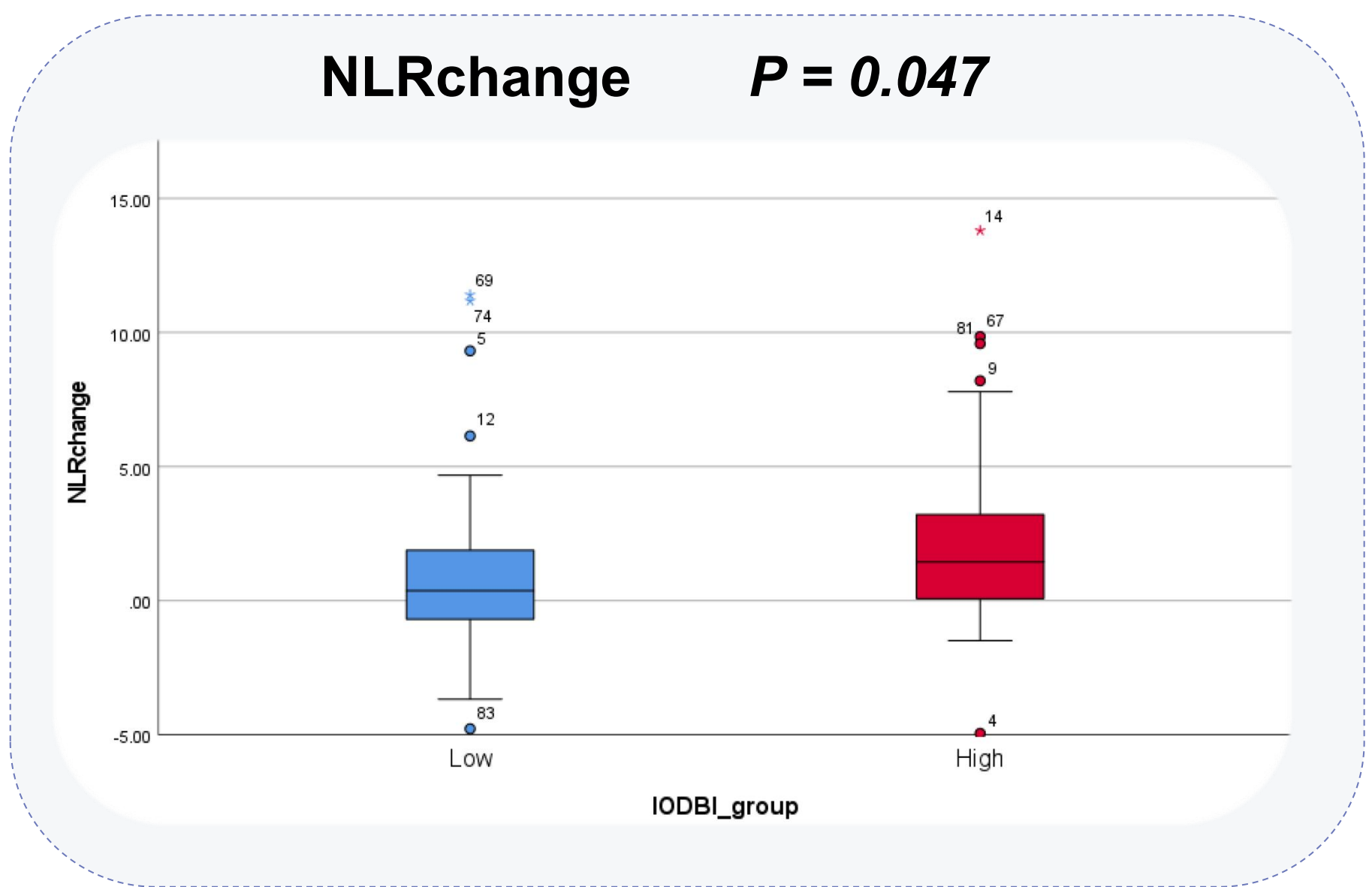
OS
High vs Low IODBI
HR = 3.02
P = 0.0005



~3-fold higher risk of death

4. Results

(4) Peripheral immune perturbation

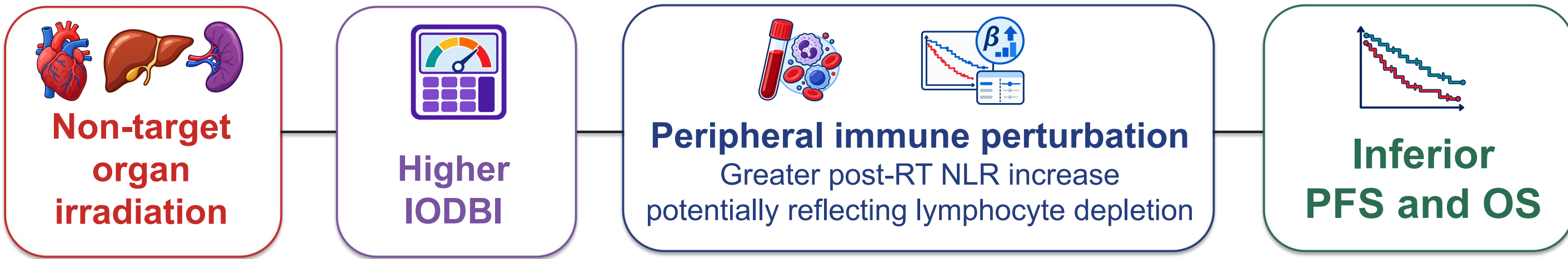


NLRchange summary, median (Q1–Q3)

Group	Median	Q1	Q3
Low IODBI (n=53)	0.373	-0.791	2.073
High IODBI (n=35)	1.447	0.032	3.253

- High immune-organ radiation burden was associated with altered post-radiotherapy peripheral immune dynamics.
- Because direct ALCchange was not statistically significant, NLRchange is interpreted as an indirect marker of peripheral immune perturbation that may, at least in part, reflect altered lymphocyte dynamics.

(5) Proposed biological model



5. Conclusions

- 1 Higher radiation exposure to the heart, liver, and spleen was associated with adverse PFS and OS.
- 2 The exploratory IODBI = 0.15 × Heart + 0.75 × Liver + 0.10 × Spleen identified a high-dose-burden subgroup with significantly worse PFS (HR = 2.01, P = 0.006) and OS (HR = 3.02, P = 0.0005).
- 3 High IODBI was also associated with a greater post-radiotherapy NLR increase (P = 0.047).

6. Discussion

- Radiation exposure to immune-relevant non-target organs may influence the efficacy of LDRT combined with chemoimmunotherapy.
- These findings suggest that immune-organ dose may deserve attention during radiotherapy planning in the immunotherapy era.
- However, the IODBI was derived exploratorily within the same pooled cohort, and NLR is an indirect immune marker; therefore, independent validation is required.

ACKNOWLEDGEMENTS

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