

Supplementary Digital Content 1, Statistical Data

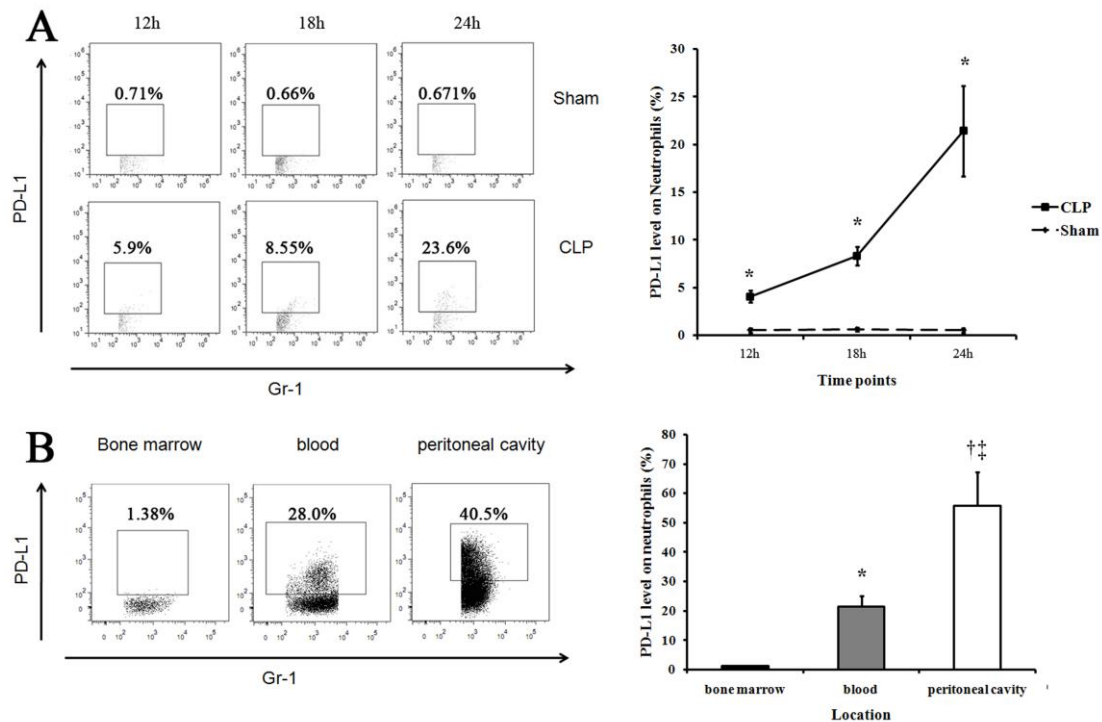


Fig. 1. PD-L1 expression on neutrophils at different time points after CLP surgery and in different locations at 24 h after surgery.

Different time points (A):

CLP vs. Sham for all time points, $p < 0.001$

CLP 12 h vs. CLP 18 h, $p=0.02$; CLP 12 h vs. 24 h, $p < 0.001$; CLP 18 h vs. CLP 24 h, $p < 0.001$.

Different location (B):

BM vs. Blood, BM vs. PC, Blood vs. PC, $p < 0.001$.

BM = bone marrow; CLP = cecal ligation puncture; PC = peritoneal cavity;

PD-L1 = programmed death receptor 1 ligand 1.

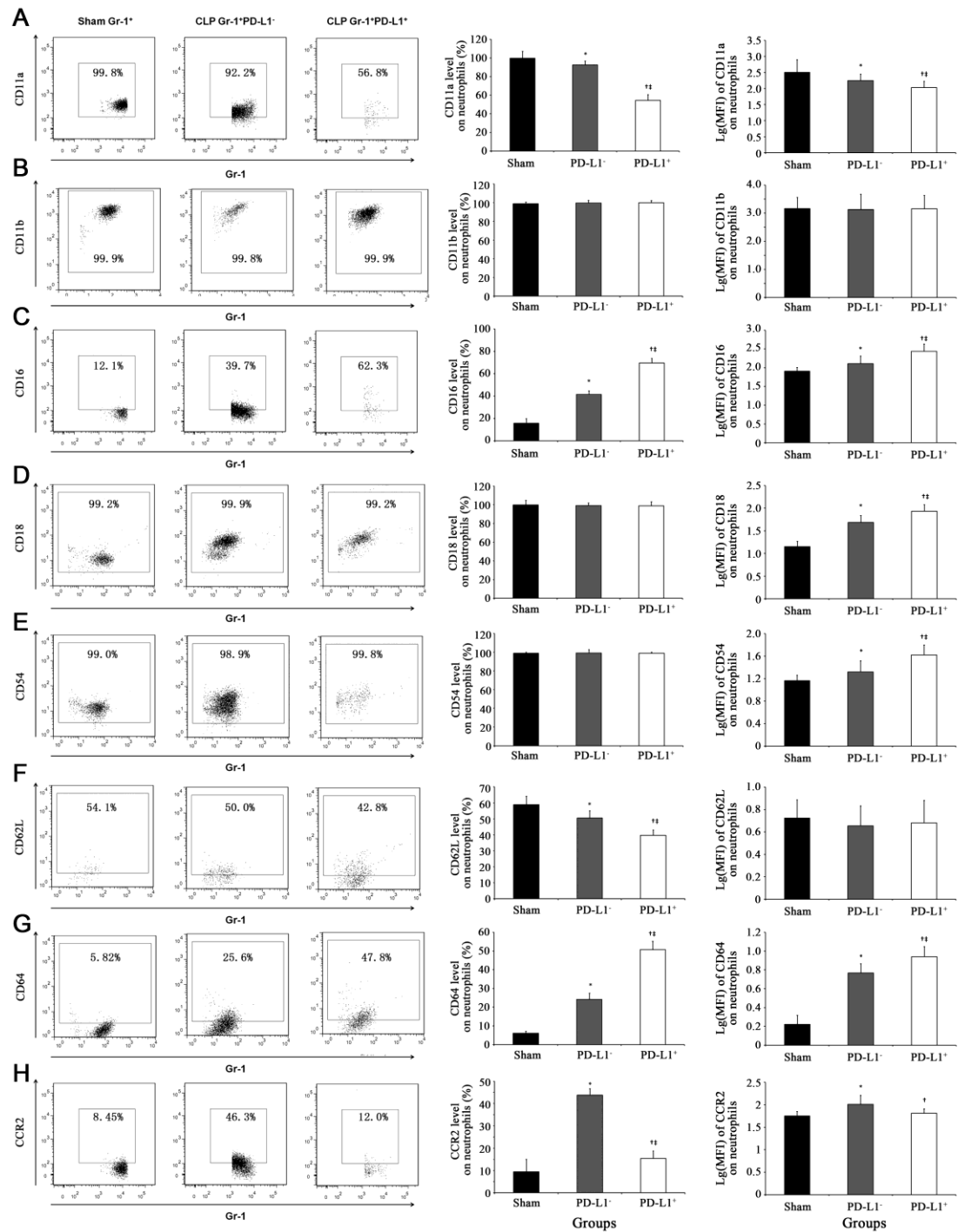


Fig. 2. Comparison of CD11a, CD11b, CD16, CD18, CD54, CD62L, CD64, and CCR2 between neutrophils from sham operated mice, PD-L1⁺ and PD-L1⁻ neutrophils from CLP mice.

Percentage:

CD11a (A): Sham vs. PD-L1⁻, $p = 0.048$; SHAM vs. PD-L1⁺, $p < 0.001$; PD-L1⁻

vs. PD-L1⁺, $p < 0.001$;

CD11b (B): Sham vs. PD-L1⁻, $p = 0.413$; SHAM vs. PD-L1⁺, $p = 0.939$; PD-L1⁻ vs. PD-L1⁺, $p = 0.457$;

CD16 (C): Sham vs. PD-L1⁻, $p < 0.001$; SHAM vs. PD-L1⁺, $p < 0.001$; PD-L1⁻ vs. PD-L1⁺, $p < 0.001$;

CD18 (D): Sham vs. PD-L1⁻, $p = 0.233$; SHAM vs. PD-L1⁺, $p = 0.725$; PD-L1⁻ vs. PD-L1⁺, $p = 0.130$;

CD54 (E): Sham vs. PD-L1⁻, $p = 1.000$; SHAM vs. PD-L1⁺, $p = 0.881$; PD-L1⁻ vs. PD-L1⁺, $p = 0.881$;

CD62L (F): Sham vs. PD-L1⁻, $p = 0.006$; SHAM vs. PD-L1⁺, $p < 0.001$; PD-L1⁻ vs. PD-L1⁺, $p = 0.001$;

CD64 (G): Sham vs. PD-L1⁻, $p < 0.001$; SHAM vs. PD-L1⁺, $p < 0.001$; PD-L1⁻ vs. PD-L1⁺, $p < 0.001$;

CCR2 (H): Sham vs. PD-L1⁻, $p < 0.001$; SHAM vs. PD-L1⁺, $p < 0.001$; PD-L1⁻ vs. PD-L1⁺, $p = 0.020$.

MFI:

CD11a (A): Sham vs. PD-L1⁻, $p = 0.041$; SHAM vs. PD-L1⁺, $p < 0.001$; PD-L1⁻ vs. PD-L1⁺, $p = 0.044$;

CD11b (B): Sham vs. PD-L1⁻, $p = 0.874$; SHAM vs. PD-L1⁺, $p = 0.960$; PD-L1⁻ vs. PD-L1⁺, $p = 0.914$;

CD16 (C): Sham vs. PD-L1⁻, $p = 0.022$; SHAM vs. PD-L1⁺, $p < 0.001$; PD-L1⁻ vs. PD-L1⁺, $p < 0.001$;

CD18 (D): Sham vs. PD-L1⁻, $p < 0.001$; SHAM vs. PD-L1⁺, $p < 0.001$; PD-L1⁻ vs. PD-L1⁺, $p = 0.006$;

CD54 (E): Sham vs. PD-L1⁻, $p = 0.044$; SHAM vs. PD-L1⁺, $p < 0.001$; PD-L1⁻ vs. PD-L1⁺, $p < 0.001$;

CD62L (F): Sham vs. PD-L1⁻, $p = 0.480$; SHAM vs. PD-L1⁺, $p = 0.652$; PD-L1⁻ vs. PD-L1⁺, $p = 0.796$;

CD64 (G): Sham vs. PD-L1⁻, $p < 0.001$; SHAM vs. PD-L1⁺, $p < 0.001$; PD-L1⁻ vs. PD-L1⁺, $p = 0.005$;

CCR2 (H): Sham vs. PD-L1⁻, $p = 0.002$; SHAM vs. PD-L1⁺, $p = 0.586$; PD-L1⁻ vs. PD-L1⁺, $p = 0.005$.

CCR2 = C-C chemokine receptor type 2; PD-L1 = programmed death receptor 1 ligand 1.

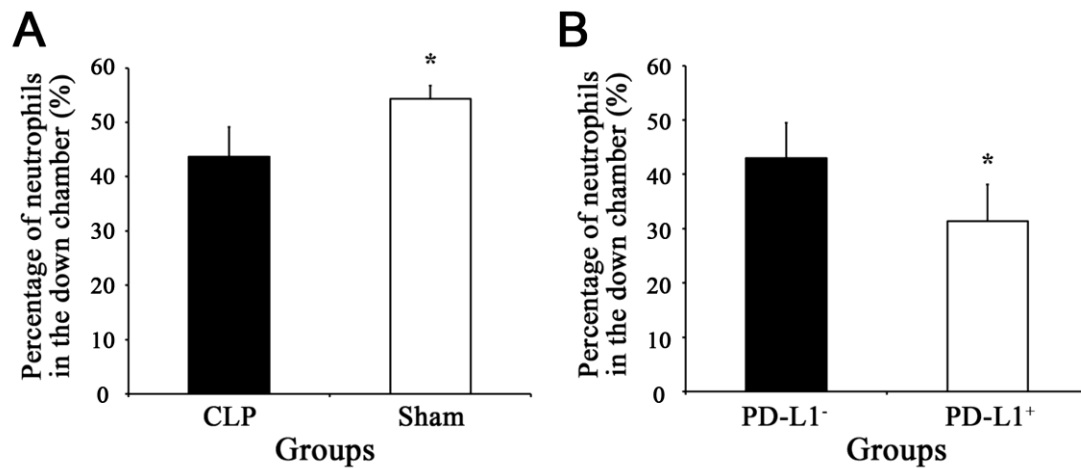


Fig. 3. Migratory ability of neutrophils isolated from sham operated mice, PD-L1⁺ and PD-L1⁻ neutrophils from CLP mice.

CLP vs. Sham, $p = 0.003$ (A); PD-L1⁺ vs. PD-L1⁻, $p = 0.013$ (B).

CLP = cecal ligation puncture; PD-L1 = programmed death receptor 1 ligand 1.

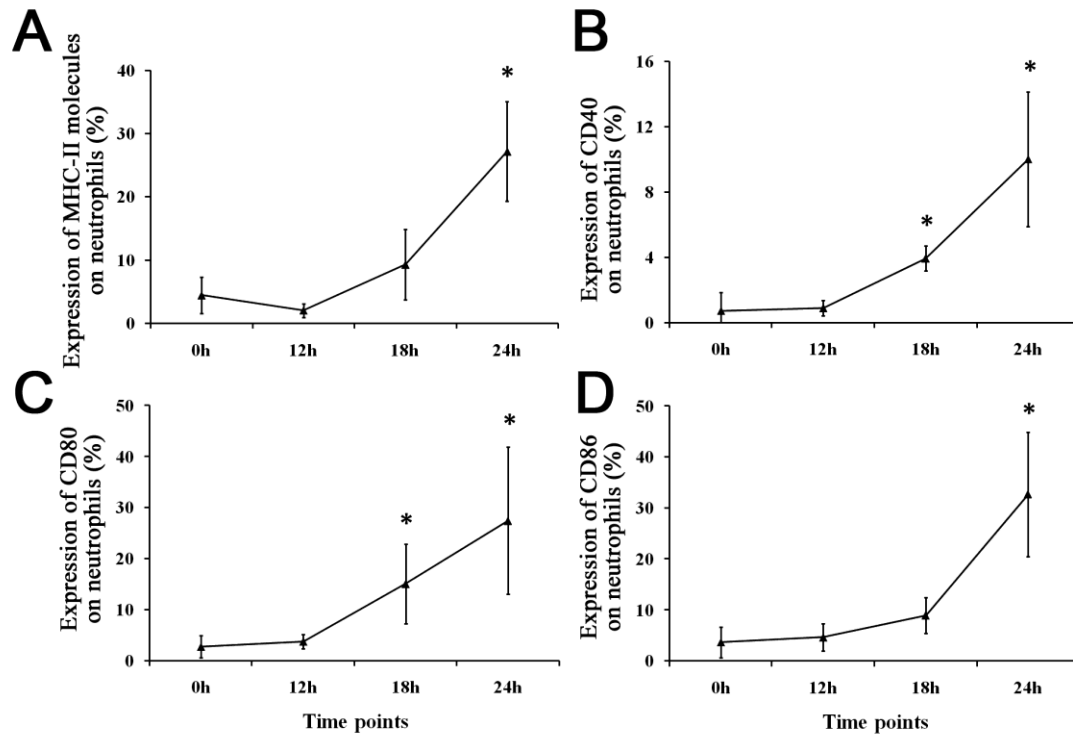


Fig. 4. Expression of MHC class II molecule, CD40, CD80, and CD86 on neutrophils isolated from CLP mice.

MHC-II (A): 0 h vs. 12 h, $p = 0.421$; 0 h vs. 18 h, $p = 0.111$; 0 h vs. 24 h, $p < 0.001$; 12 h vs. 18 h, $p = 0.022$; 12 h vs. 24 h, $p < 0.001$; 18 h vs. 24 h, $p < 0.001$;
 CD40 (B): 0 h vs. 12 h, $p = 0.907$; 0 h vs. 18 h, $p = 0.019$; 0 h vs. 24 h, $p < 0.001$;
 12 h vs. 18 h, $p = 0.025$; 12 h vs. 24 h, $p < 0.001$; 18 h vs. 24 h, $p < 0.001$;
 CD80 (C): 0 h vs. 12 h, $p = 0.831$; 0 h vs. 18 h, $p = 0.018$; 0 h vs. 24 h, $p < 0.001$;
 12 h vs. 18 h, $p = 0.029$; 12 h vs. 24 h, $p < 0.001$; 18 h vs. 24 h $p = 0.018$;
 CD86 (D): 0 h vs. 12 h, $p = 0.807$; 0 h vs. 18 h, $p = 0.185$; 0 h vs. 24 h, $p < 0.001$;
 12 h vs. 18 h, $p = 0.273$; 12 h vs. 24 h, $p < 0.001$; 18 h vs. 24 h $p < 0.001$.

CLP = cecal ligation puncture; MHC = major histocompatibility complex.

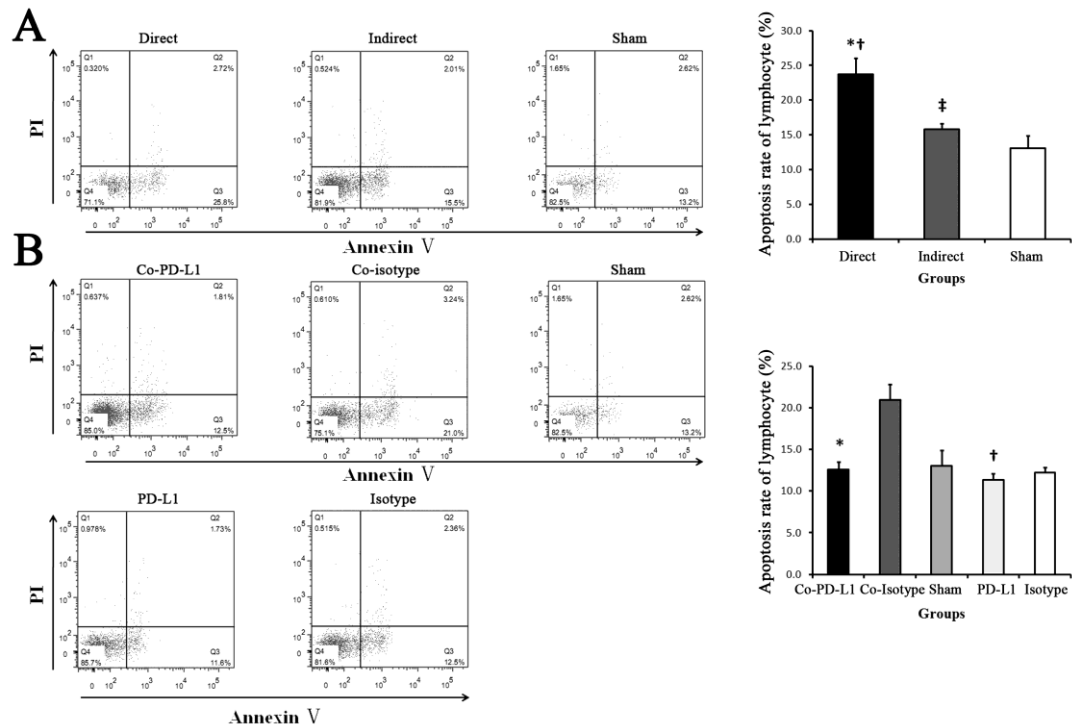


Fig. 5. Influence of PD-L1 on neutrophils from CLP mice on lymphocyte apoptosis.

A. Direct vs. Indirect, $p < 0.001$; Direct vs. Sham, $p < 0.001$; Indirect vs. Sham, $p = 0.015$;

B. Co-PD-L1 vs. Co-Isotype, $p < 0.001$; Co-PD-L1 vs. Sham, $p = 0.530$;
 Co-PD-L1 vs. PD-L1, $p = 0.117$; Co-PD-L1 vs. Isotype, $p = 0.633$; Co-Isotype vs. Sham, $p < 0.001$; Co-Isotype vs. PD-L1, $p < 0.001$; Co-Isotype vs. Isotype, $p < 0.001$; Sham vs. PD-L1, $p = 0.033$; Sham vs. Isotype, $p = 0.273$; PD-L1 vs. Isotype, $p = 0.264$.

CLP = cecal ligation puncture; PD-L1 = programmed death receptor 1 ligand 1.

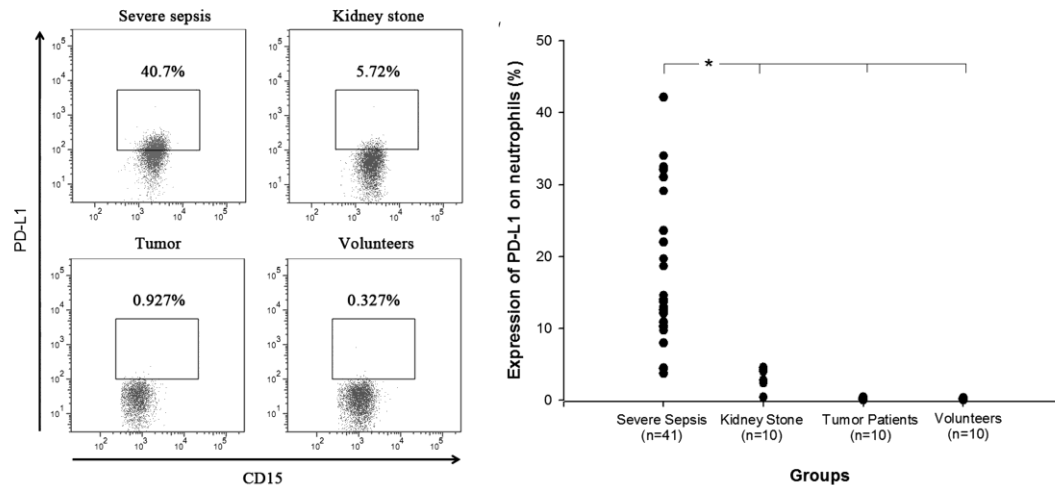


Fig. 6. PD-L1 expression on neutrophils from patients with severe sepsis, sepsis after PCNL for infectious kidney stone, tumor and healthy volunteers.

Severe sepsis vs. Kidney stone, $p = 0.009$; Severe sepsis vs. Tumor patients $p < 0.001$; Severe sepsis vs. Volunteers, $p < 0.001$; Kidney stone vs. Tumor patients $p = 0.550$; Kidney stone vs. Volunteers, $p = 0.314$; Tumor patients vs. Volunteers, $p = 0.980$.

PCNL = percutaneous nephrolithotomy; PD-L1 = programmed death receptor 1 ligand 1.

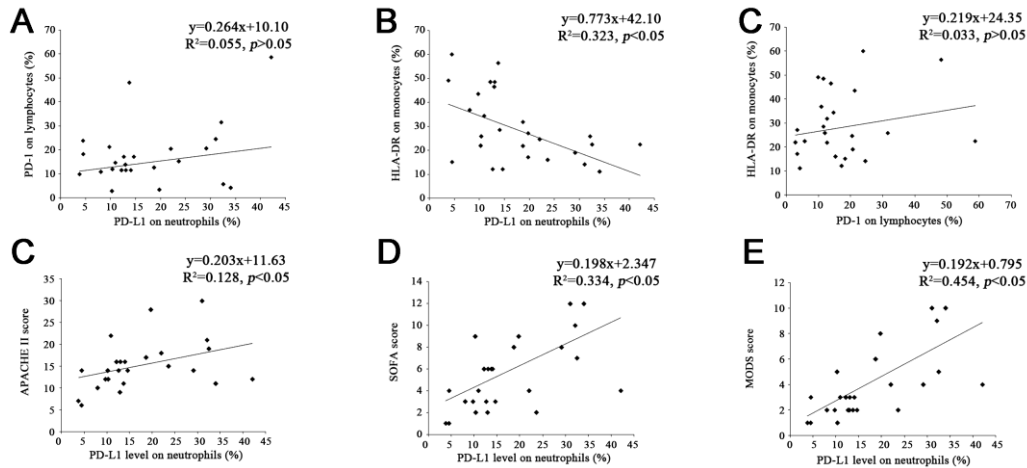


Fig. 7. The correlation of neutrophil PD-L1 with marker of immunosuppression and disease severity by linear regression analysis.

A. Neutrophil PD-L1 & Lymphocyte PD-1, $p = 0.139$; B. Neutrophil PD-L1 & Monocyte HLA-DR, $p = 0.010$; C. Lymphocyte PD-1 & Monocyte HLA-DR, $p = 0.255$. D. Neutrophil PD-L1 & APACHE II score, $p = 0.021$; E. Neutrophil PD-L1 & SOFA score, $p < 0.001$; F. Neutrophil PD-L1 & MODS, score $p < 0.001$.

APACHE = acute physiology and chronic health evaluation; HLA-DR = human leukocyte antigen DR; MODS = multiple organ dysfunction syndrome; PD-1 = programmed death receptor 1; PD-L1 = programmed death receptor 1 ligand 1; SOFA = sequential organ failure assessment.

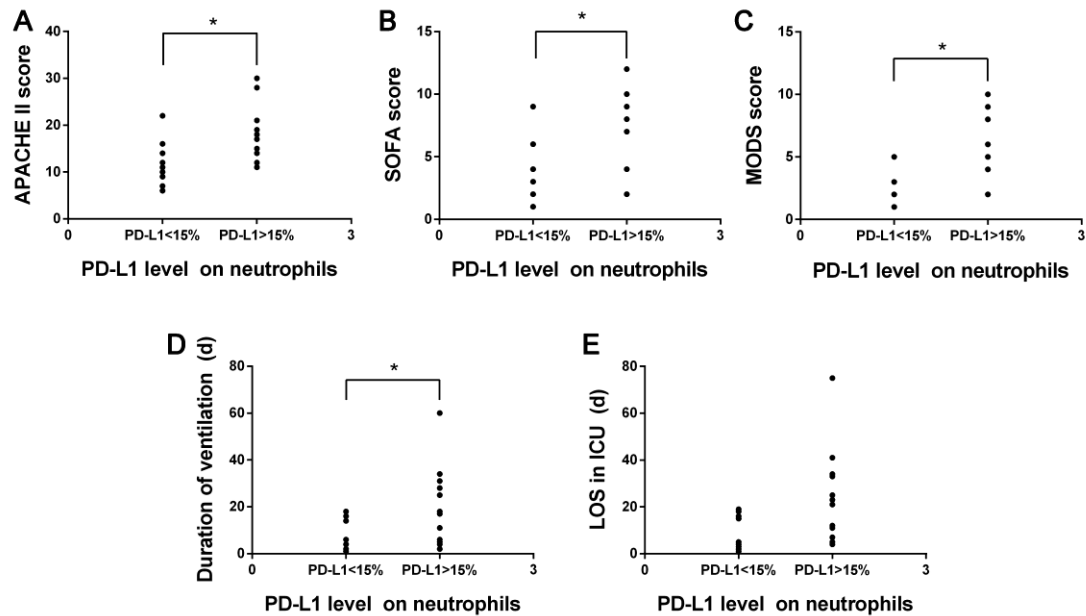


Fig. 8. Disease severity, duration of mechanical and LOS in ICU in patients with different PD-L1 level on neutrophils.

* $p < 0.05$ by Mann-Whitney U test.

A. APACHE II score, $p = 0.002$; B. SOFA score, $p = 0.001$; C. MODS score, $p < 0.001$; D. mechanical ventilation, $p = 0.033$; E. LOS, $p = 0.060$.

APACHE = acute physiology and chronic health evaluation; HLA-DR = human leukocyte antigen DR; ICU = intensive care unit; LOS = length of stay; MODS = multiple organ dysfunction syndrome; PD-L1 = programmed death receptor 1 ligand 1; SOFA = sequential organ failure assessment.