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BACKGROUND:

Our previous data indicated that fibrinogen (FIB) and fresh frozen plasma (FFP) administration mitigates lung dysfunction in mice after trauma and hemorrhagic shock (HS), due in part to restoring endothelial syndecan-1 (Sdc1)/glycocalyx. Further, we found that fibrinogen, the major component of plasma, is capable of binding to Sdc1 to prevent Sdc1 shedding and maintain the endothelial barrier. As pulmonary infection is reportedly a common complication following severe trauma, we sought to investigate the potential therapeutic effects of fibrinogen and FFP in this combined model.

RESULTS:

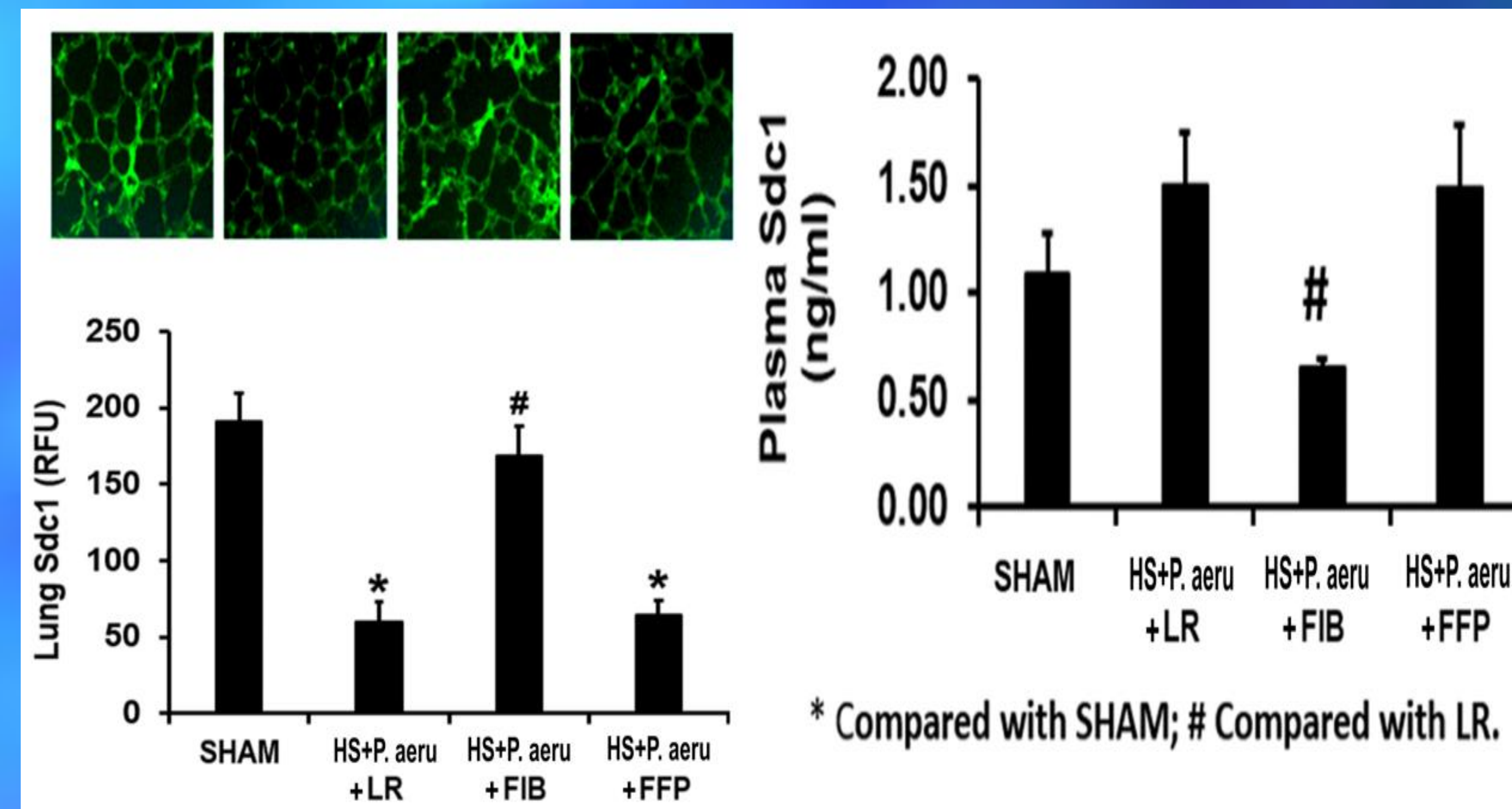


Fig 1. Left: Syndecan-1 immunofluorescent staining showed that, compared with SHAM, HS+P aeruginosa decreased syndecan-1 staining. Resuscitation with fibrinogen restored the cell surface syndecan-1 to normal levels. However, FFP showed no effect. Right: Compared with SHAM, HS+P. aeruginosa increased plasma syndecan-1 levels. Resuscitation with fibrinogen decreased the plasma syndecan-1. Again, FFP showed no effect.

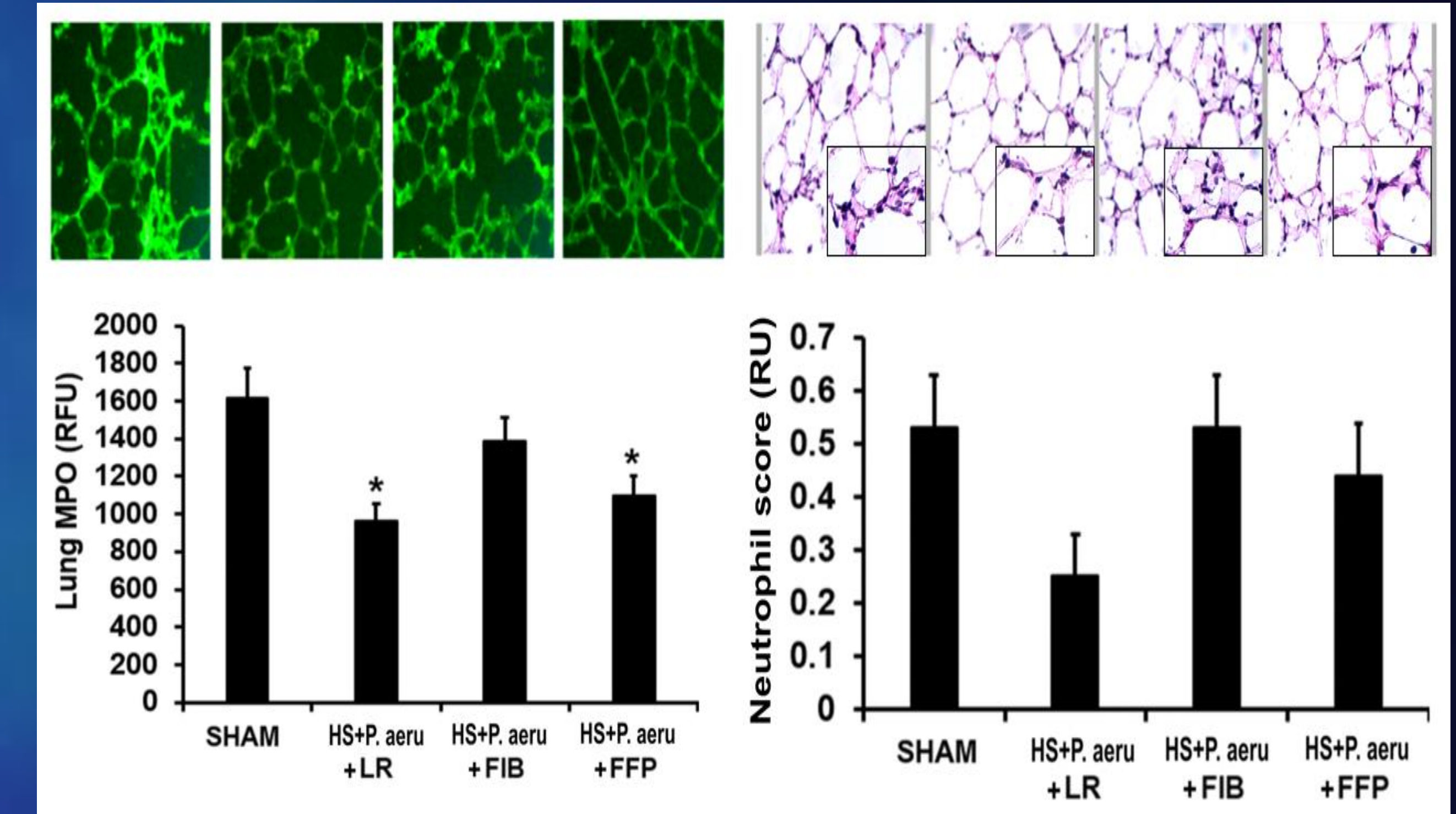
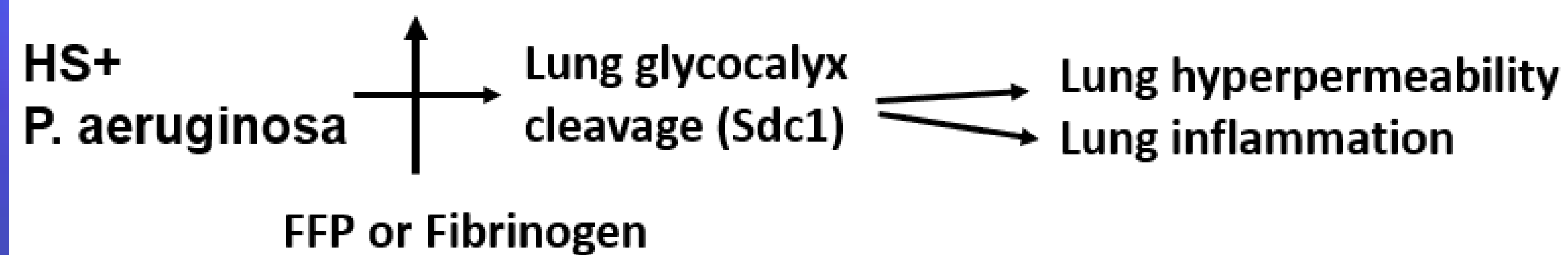
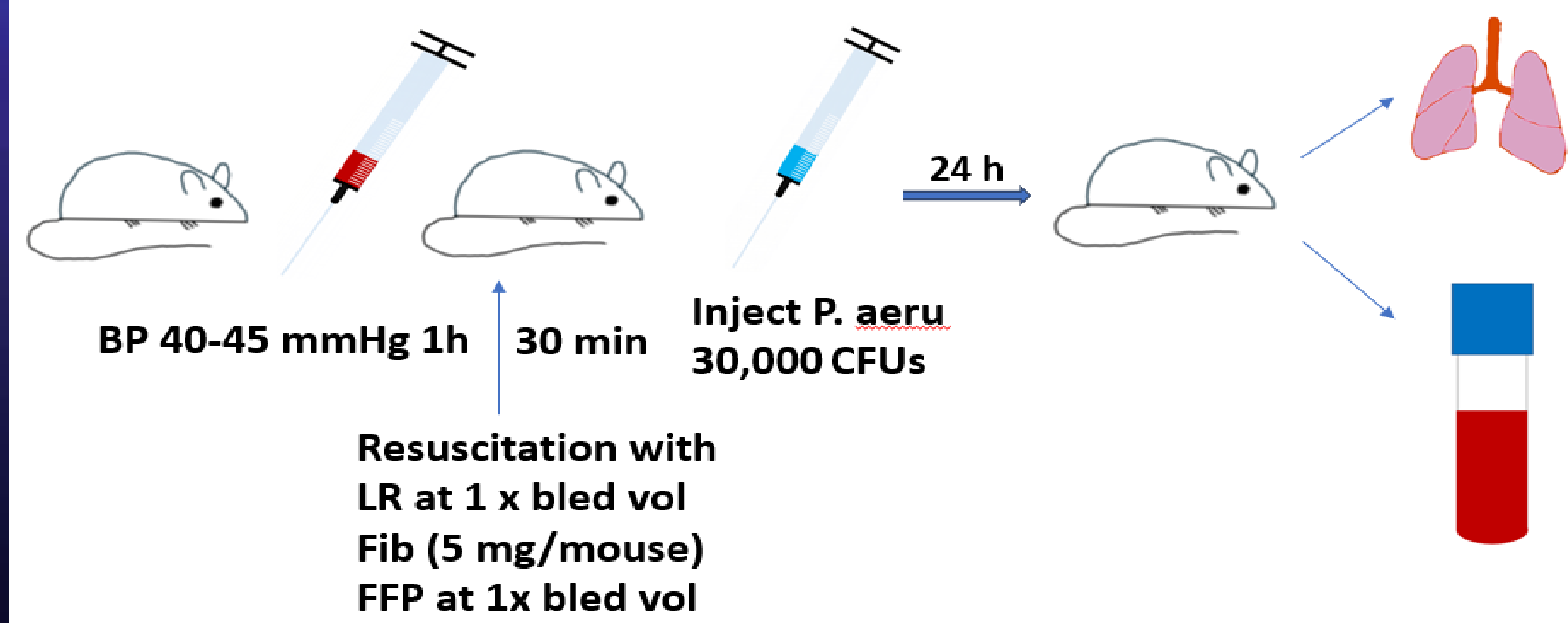


Fig 3. Left: MPO immunofluorescent staining results indicated that, compared with SHAM, HS+P. aeruginosa induced a significant decrease on MPO staining. Fibrinogen resuscitation prevented this decrease, but FFP showed no effect. Right: H&E staining results indicated that, compared with SHAM, HS+P. aeruginosa decreased the neutrophil infiltration. Fibrinogen resuscitation tends to prevent this decrease. FFP showed no obvious effect.

HYPOTHESIS



METHODS



METHODS: BAL protein was measured as an indicator for lung permeability. Lung inflammation was assessed by myeloperoxidase (MPO) and neutrophil staining. Plasma Sdc1 was measured by ELISA. Data were analyzed using one-way ANOVA with Bonferroni correction; n= 8/group.

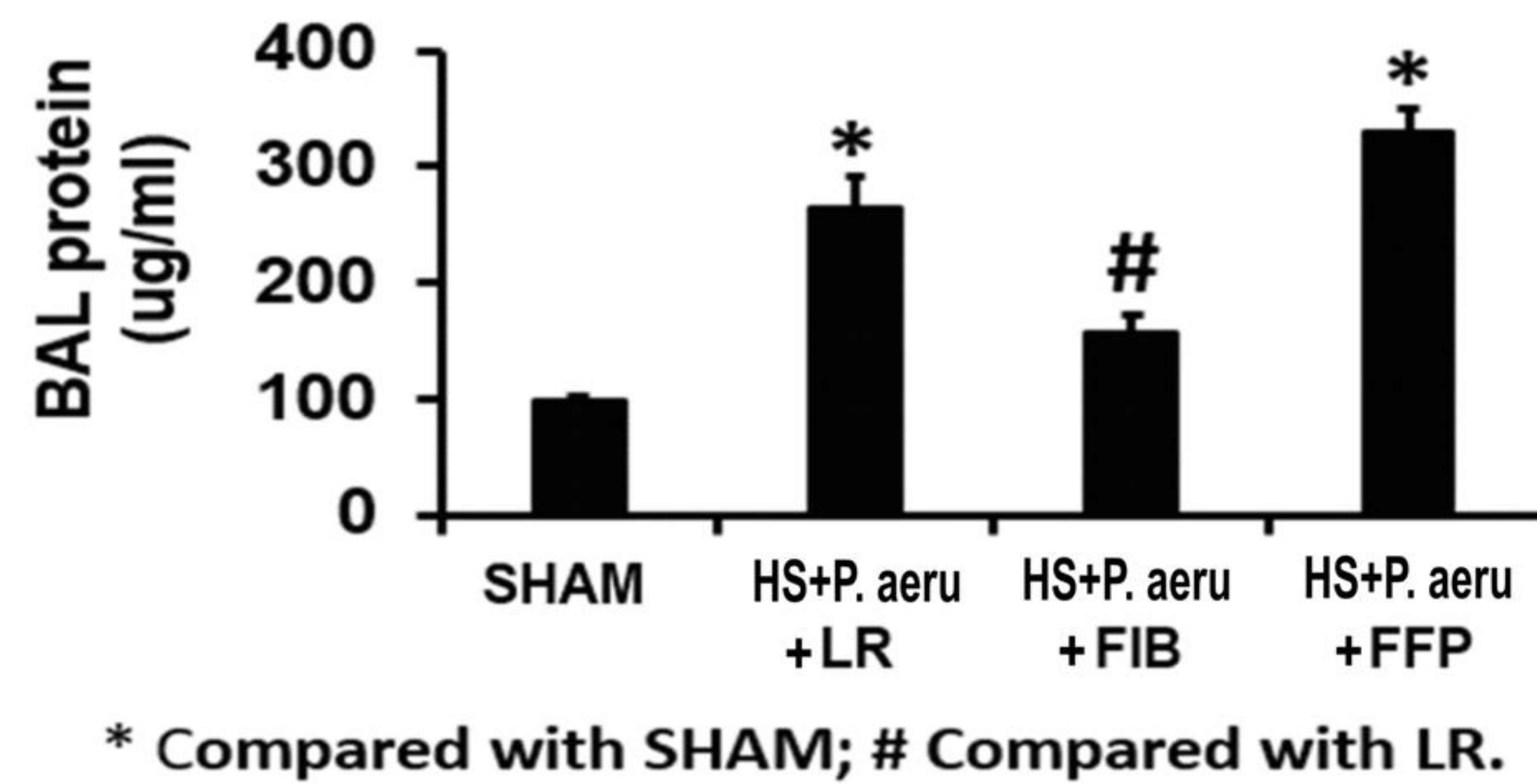
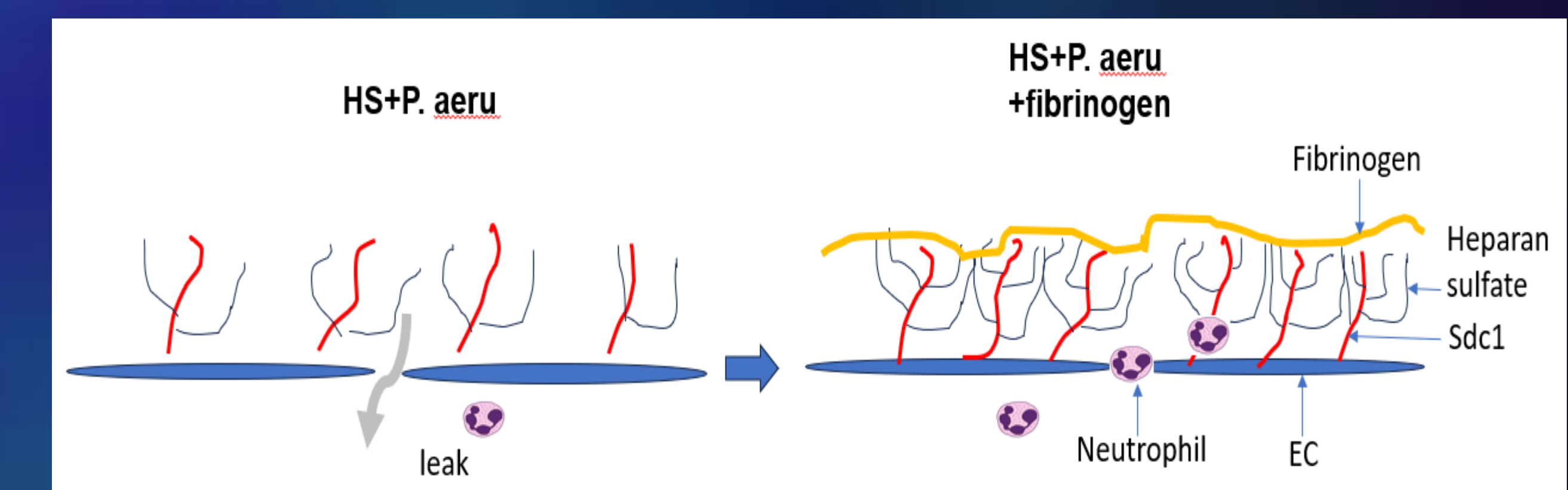


Fig 2. Compared with SHAM, HS+P. aeruginosa caused a significant increase in BAL protein concentrations. Fibrinogen resuscitation attenuated the BAL protein increase compared to LR group, whereas FFP has no effect.



CONCLUSION

- HS+ P. aeruginosa caused syndecan-1 shedding and lung hyperpermeability reversed only by fibrinogen.
- HS+ P. aeruginosa led to a lung innate immunity deficiency state lessened only by fibrinogen.
- Taken together, these results suggest that fibrinogen has a therapeutic benefit beyond hemostasis.

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