

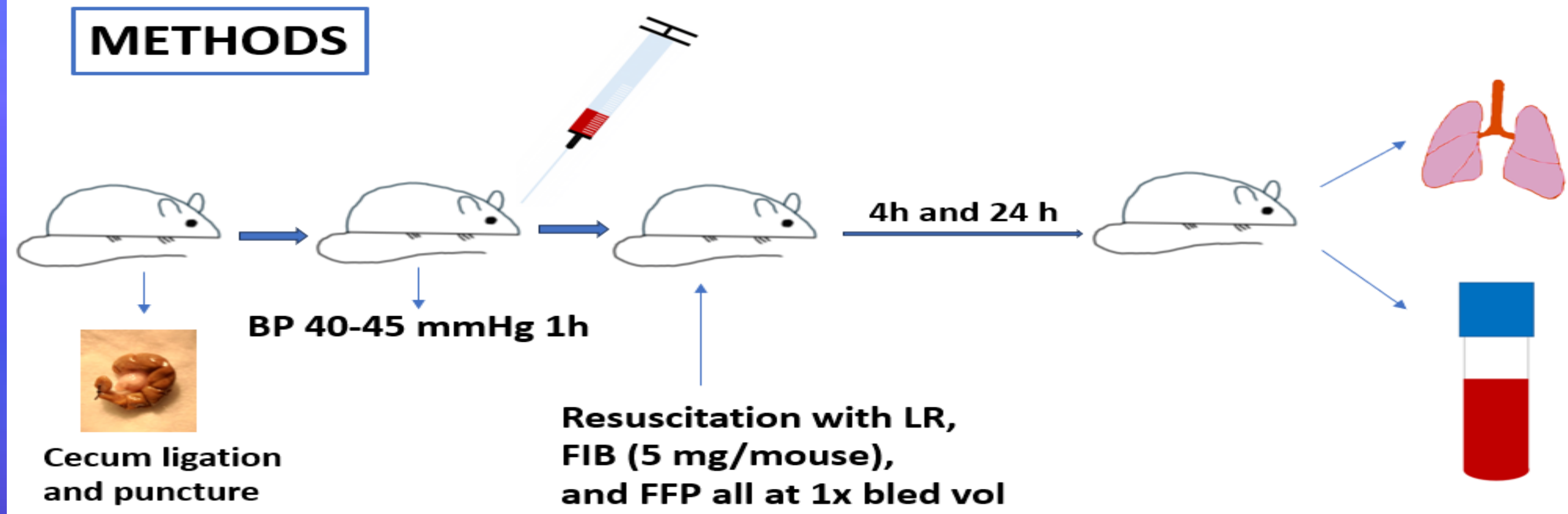
Feng Wu, Jody Cantu, Rosemary A Kozar

Shock Trauma Center and Shock Trauma Anesthesiology Research (STAR) Center, University of Maryland School of Medicine, Baltimore, MD

BACKGROUND:

Our previous study demonstrated that fibrinogen (FIB) and fresh frozen plasma (FFP) administration mitigated lung dysfunction in mice after trauma and hemorrhagic shock (HS), due in part to restoring endothelial syndecan-1 (Sdc1)/glycocalyx. Sepsis is the leading cause of death in intensive care units and remains a major cause of morbidity after trauma and shock. The optimal treatment of sepsis remains unclear. In the present study, we sought to investigate the potential therapeutic effects of FIB and FFP in a mouse model of cecal ligation and puncture (CLP) and hemorrhage shock (HS). We hypothesized that both would be equally effective in protecting lung endothelial function.

METHODS



Research was conducted in accordance with an approved animal use protocol at an AAALAC International-accredited facility, in full compliance with all applicable federal statutes and regulations governing the use of animals in research. The study adhered to the principles outlined in the Guide for the Care and Use of Laboratory Animals (National Research Council, 2011 edition)

Assays: Soluble Sdc1 (ELISA) and BAL protein (BCA assay) were measured as indicators of lung injury. Sdc1 sheddase MMP9 in plasma was measured by ELISA. Lung myeloperoxidase (MPO) was stained by immunofluorescence and plasma MPO was measured by ELISA. Data were analyzed using one-way ANOVA followed by Tukey's post hoc test; n= 8/group.

CONCLUSION:

FFP, but not FIB-resuscitation, attenuated increases in plasma Sdc1 and lung permeability, suggesting only FFP is able to protect lung endothelial function. Additionally, MAP was partially restored by FFP, but not FIB. Further, FFP, but not FIB, inhibited plasma MMP9 and MPO and increased lung MPO, implicating that FFP acts through decreasing leukocyte-derived MMP9 in circulation.

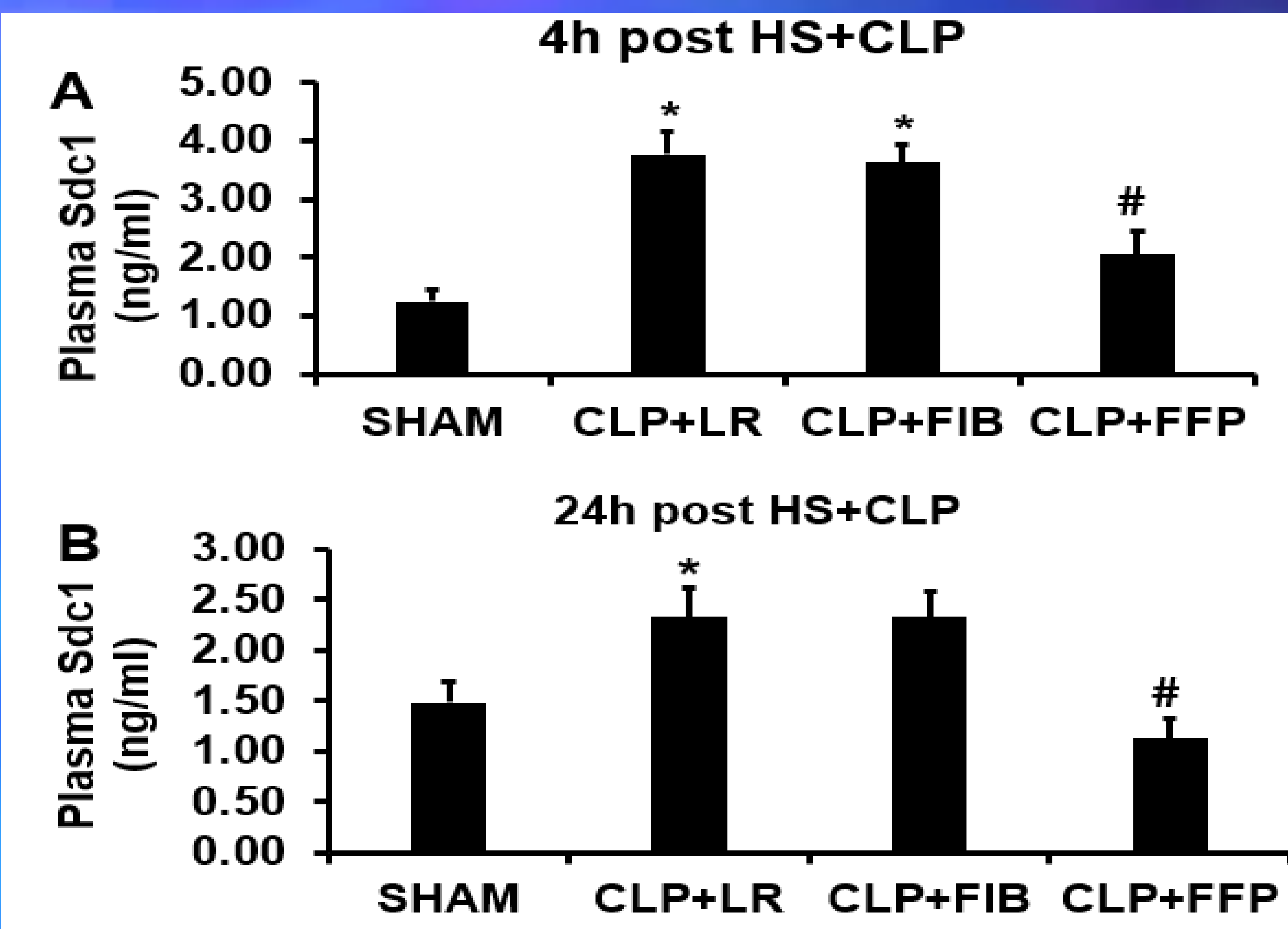


Fig 1. FFP-, but not FIB-resuscitation, attenuated soluble shed syndecan-1 at 4h (A) and 24h (B). LR: CLP+HS+lactated Ringer's solution; FIB: CLP+HS+fibrinogen; FFP: CLP+HS+fresh frozen plasma. * compared with SHAM, p<0.05; # compared with LR, p<0.05.

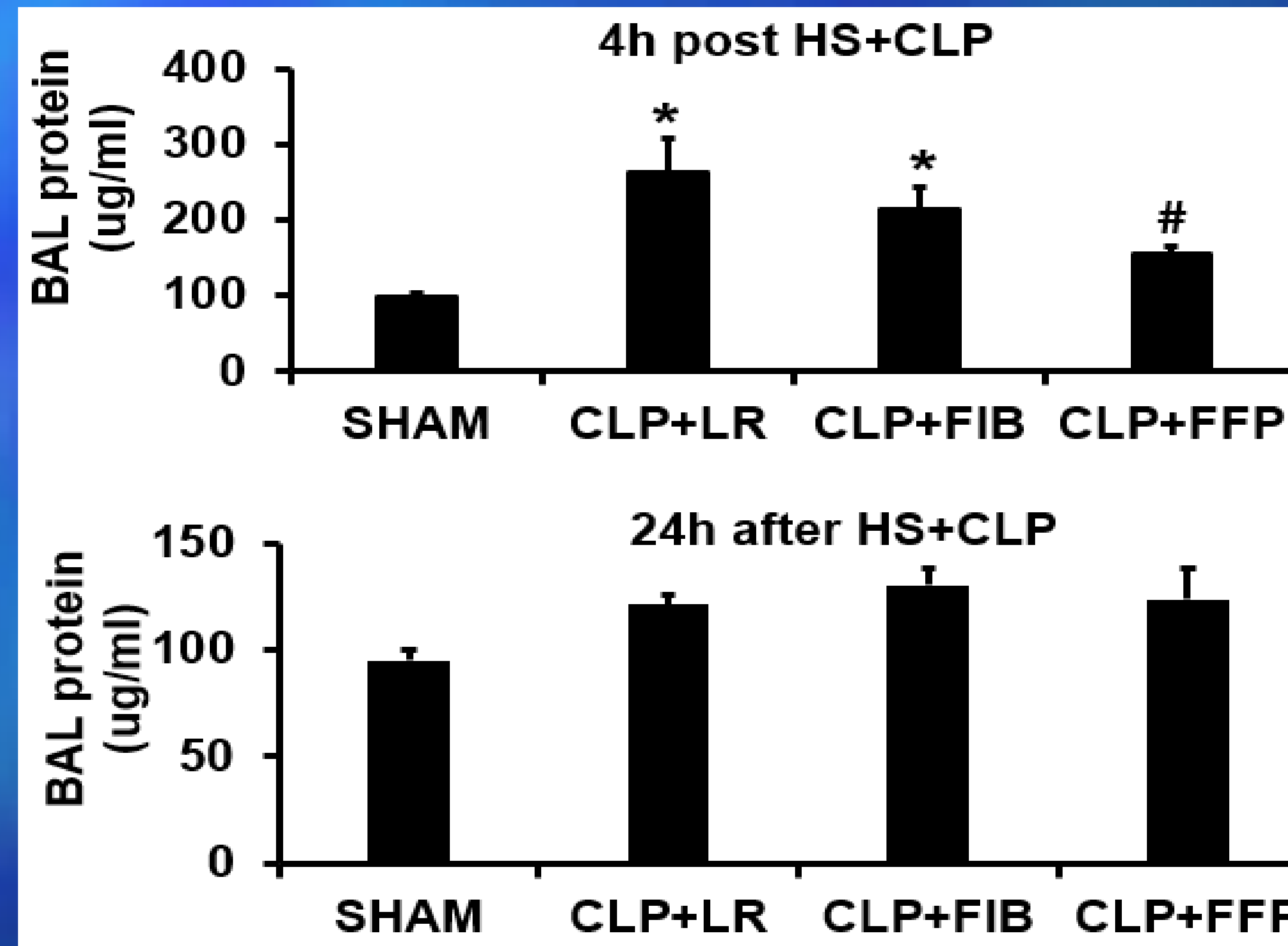


Fig 2. FFP-, but not FIB-resuscitation, attenuated increased BAL protein levels at 4h (A). There was no significant difference among the groups at 24h post CLP+HS (B).

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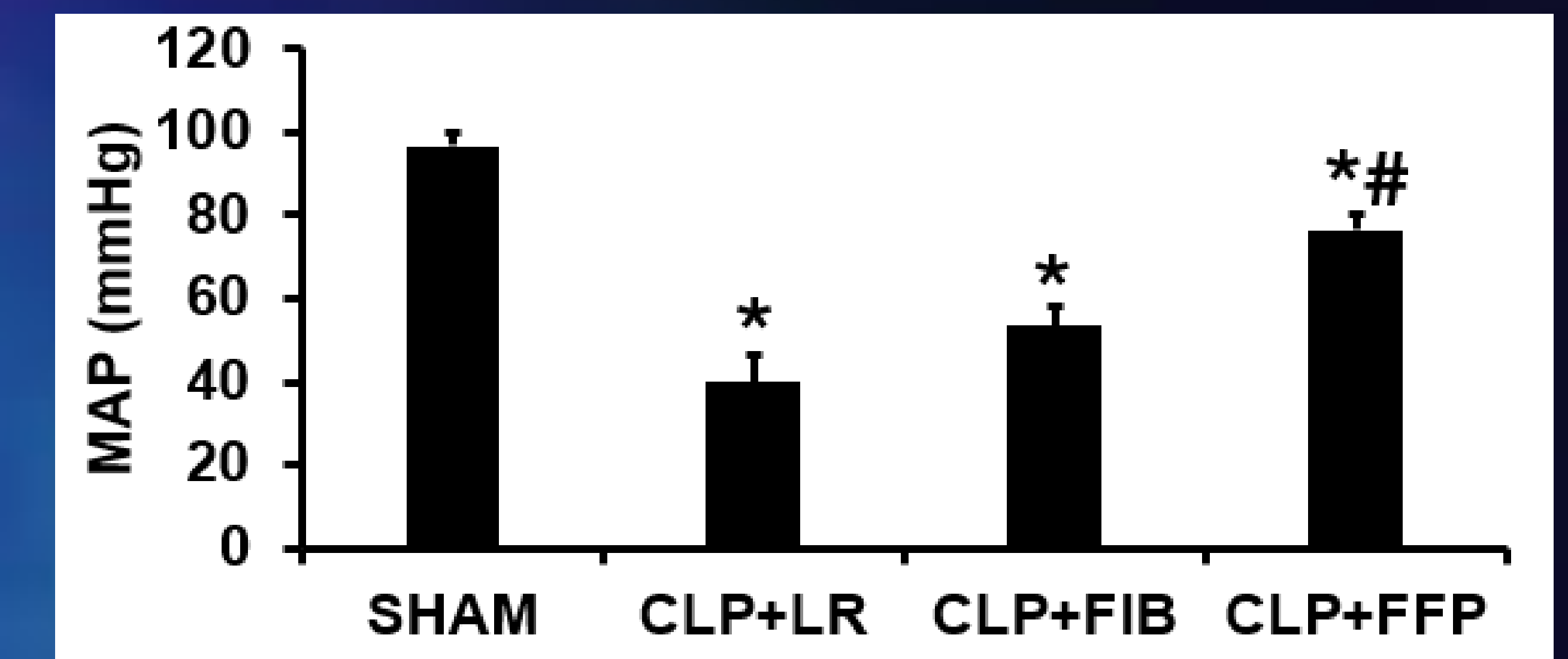


Fig 3. FFP-, but not FIB-resuscitation, increased MAP in mice post HS+CLP at 24h.

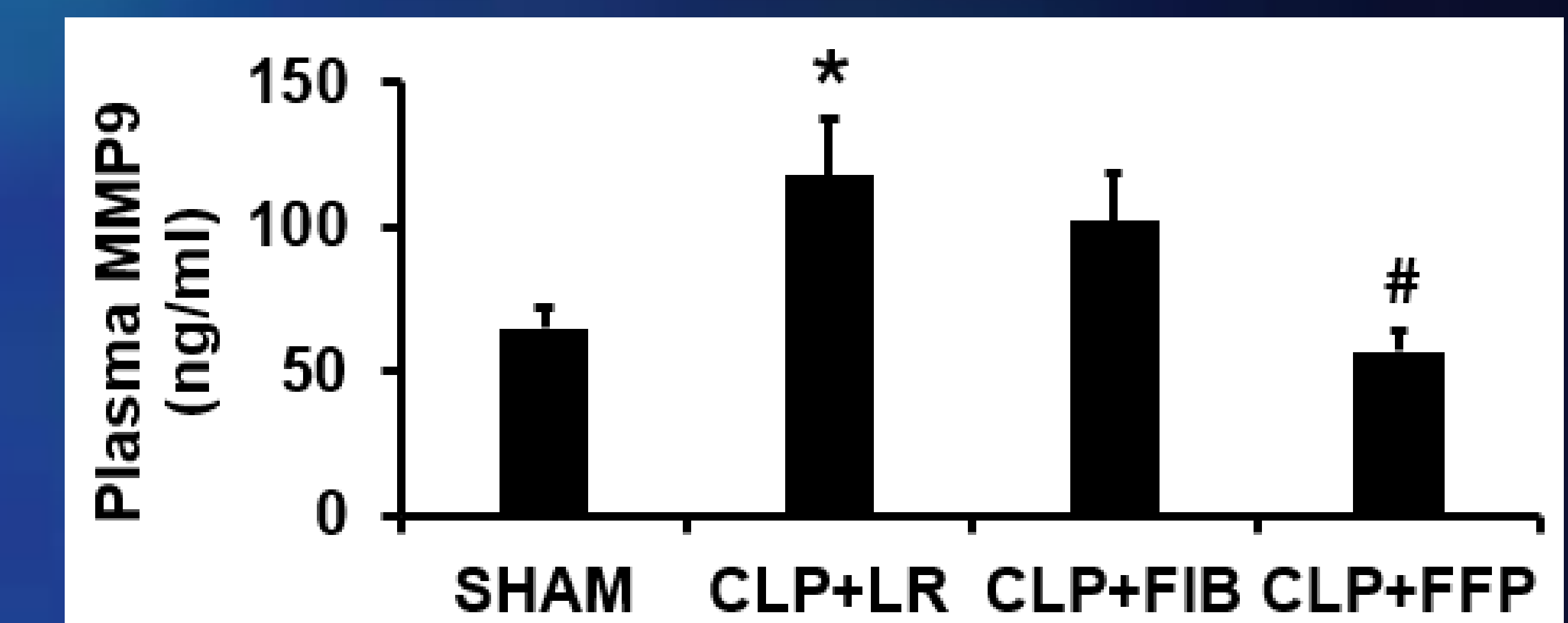


Fig 4. FFP-, but not FIB-resuscitation, attenuated the increased MMP9 in mice post HS+CLP at 24h.

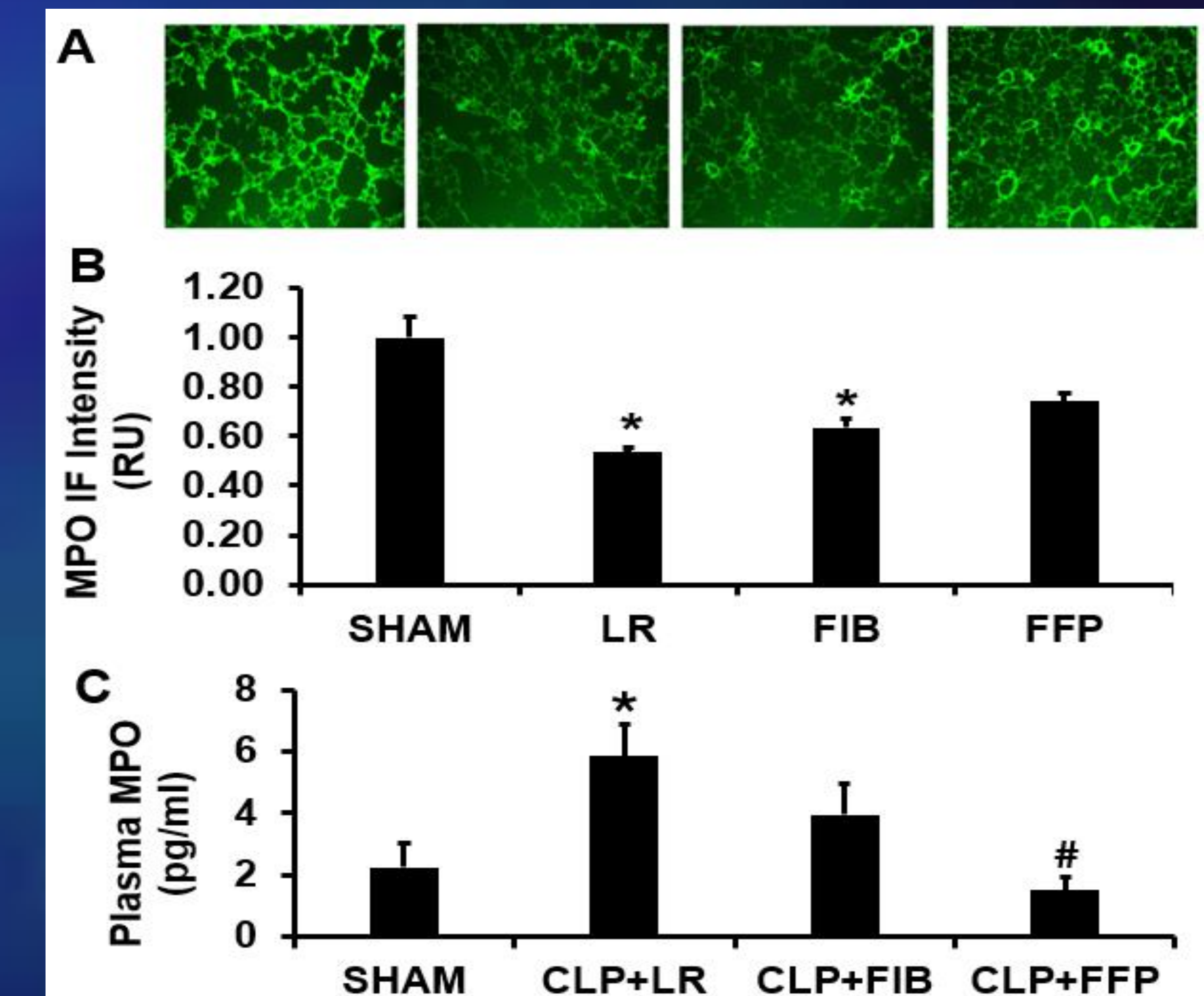


Fig 5. FFP, but not FIB, partially restored lung MPO immunostaining and significantly decreased plasma MPO levels. A. Representative lung MPO immunostaining. B. Quantification of lung MPO immunofluorescent intensity. C. Plasma MPO levels.