Characterizing Vascular Endotheliopathy Associated with Partial Versus Full REBOA in a Hemorrhagic Shock Model: A Pilot Study

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Study Objectives

- Quantify extent of endotheliopathy in a hemorrhagic-shock swine model
  - Partial REBOA (p-REBOA) vs. Full REBOA (f-REBOA)

- Understand the longitudinal change, over the study course, in:
  - Endothelial glycocalyx biomarkers, **Hyaluronic Acid (HA) and Syndecan-1 (SDC-1).**

  - Inflammatory Markers, (9-plex porcine inflammatory kit), **INF-a, INF-g, IL-1b, IL-4, IL-6, IL-8, IL-10, IL-12/IL-23p40, TNF-a**

Background

- Traumatic injuries → 5 million deaths per year globally
  - Hemorrhagic shock → 30-40% of all potentially preventable trauma-related fatalities.[1]
- Resuscitative Endovascular Balloon Occlusion of the Aorta (REBOA) →
  - Lifesaving intervention
  - Minimize major distal hemorrhage by temporarily occluding the aorta with a balloon catheter.[1]
- REBOA → high risk and associated with profound ischemia reperfusion injury (IRI).[1,2]

Background

- To minimize IRI, partial inflation of the balloon (**p-REBOA**) has been adopted.[3]
- p-REBOA reduces IRI
  - The effect of partial occlusion on the vascular endothelium and molecular level remains relatively unknown.[1,3]
- Altered hemodynamics imposed by REBOA → shear and/or ischemia-induced shedding of the endothelial glycocalyx layer
  - SHINE = shock-induced endotheliopathy.[4,5]
- **Hypothesis:** p-REBOA leads to less shock-induced endotheliopathy compared to f-REBOA in a hemorrhagic shock swine model when looking specifically at endothelial markers (**HA** and **SDC-1**) and inflammatory markers.

Methods

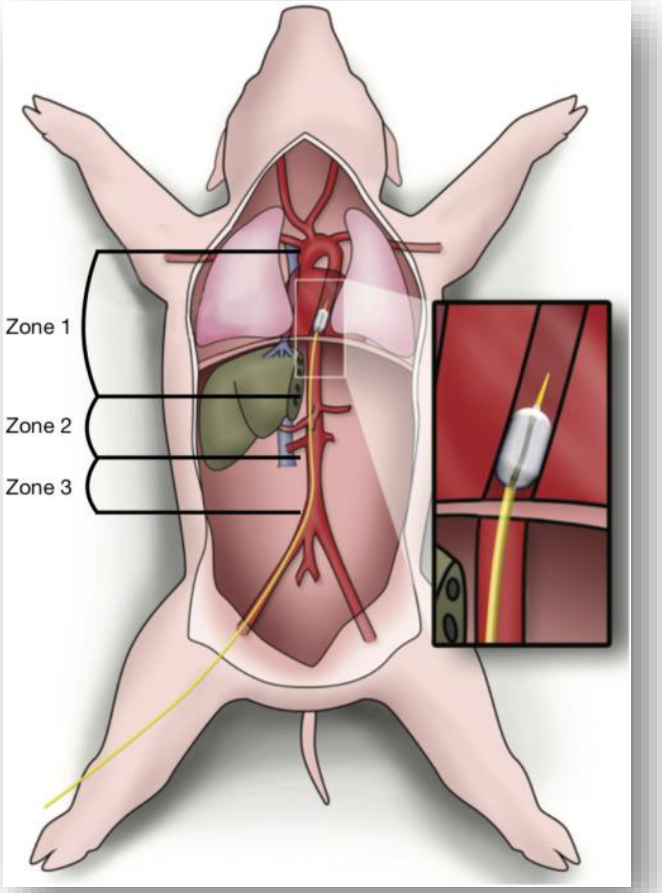

Figure 1. Illustration of Swine Experiment.[6]
REBOA catheter placed in Zone 1.

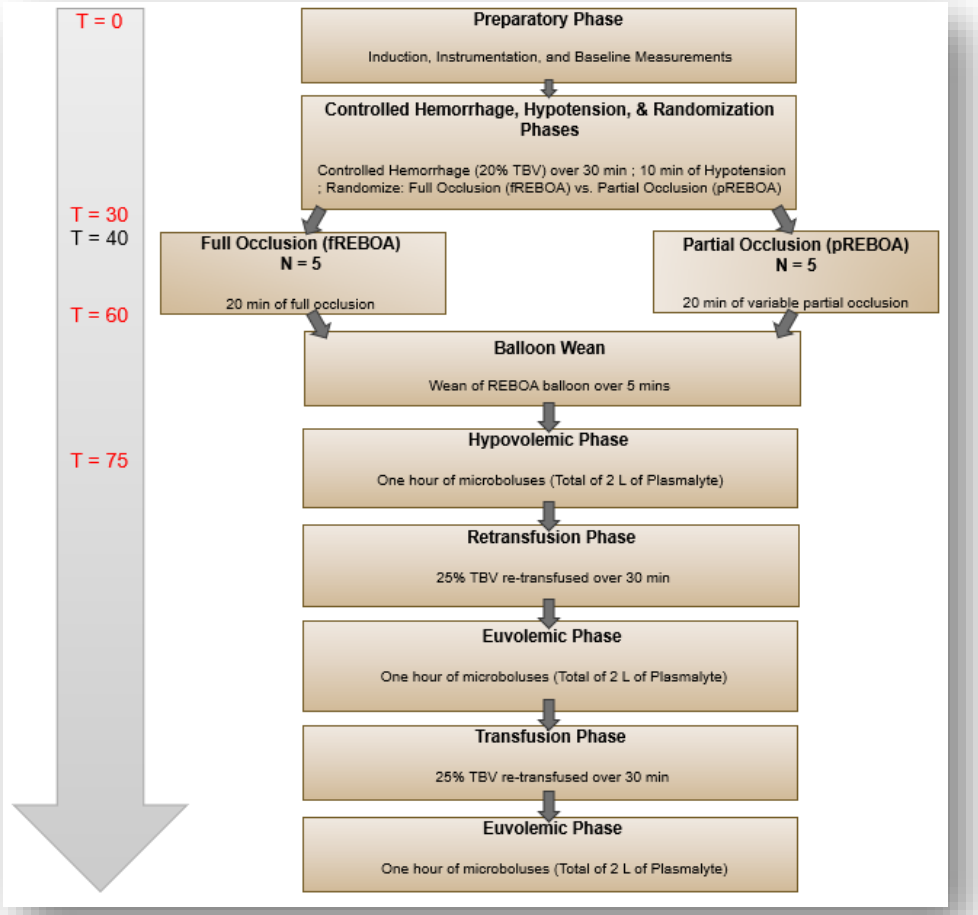

Figure 2. Study Timeline. Ten swine split into 2 groups (p-REBOA vs. f-REBOA). REBOA catheter placed in Zone 1.

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Methods

- Serum was serially collected and frozen at -80C
- Endothelial Glycocalyx Biomarkers
  - **Syndecan-1 (SDC-1)**
  - **Hyaluronic Acid (HA)**
  - ELISA kits
- Inflammatory Cytokines
  - **INF-a , INF-g, IL-1b, IL-4, IL-6, IL-8, IL-10, IL-12/IL-23p40,TNF-a**
  - 9-plex Luminex ProcartaPlex Kits for pigs
- Statistical Analysis
  - Repeated Measures ANOVA

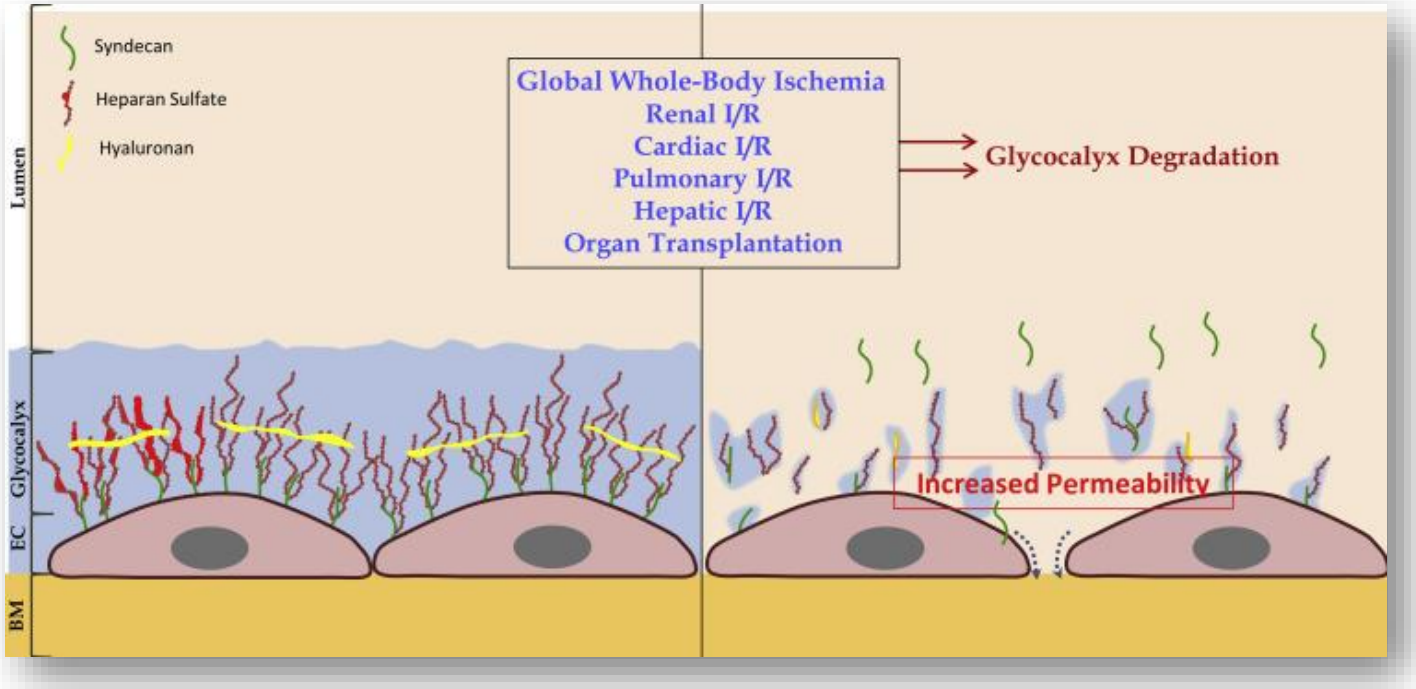

Figure 3. Schematic illustrating SHINE with ischemia reperfusion (I/R) injury and shedding of endothelial glycocalyx.[7]

Results: Hyaluronic Acid (HA)

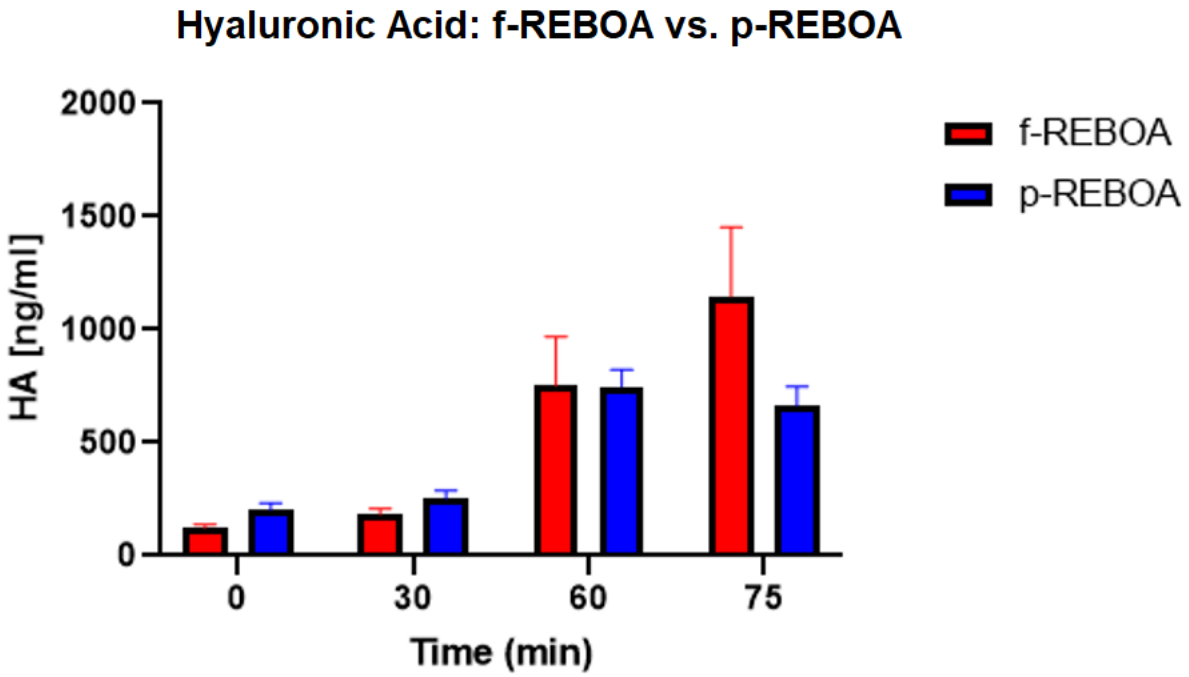

Figure 4. Serum hyaluronic Acid (HA) levels over course of study differentiated by f-REBOA vs. p-REBOA

Additional Graphs and Figures

- Increase in circulating HA levels with the introduction of both f- and p-REBOA.
  - Significant change over time, $p < 0.0001$
- No significant difference in HA between groups ($p > 0.05$)
  - f-REBOA trends to have higher shed HA at t=75 minutes (Post-occlusion), p=0.08
  - High variance in f-REBOA group may contribute to non-statistically significant finding

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Results: Syndecan-1 (SDC-1)

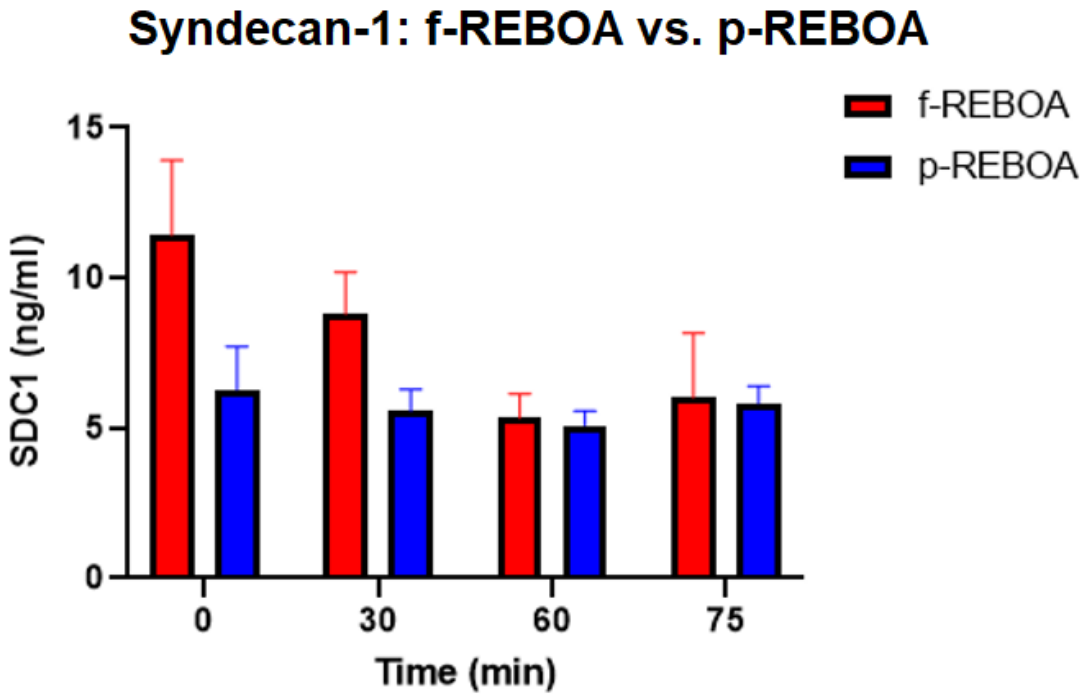


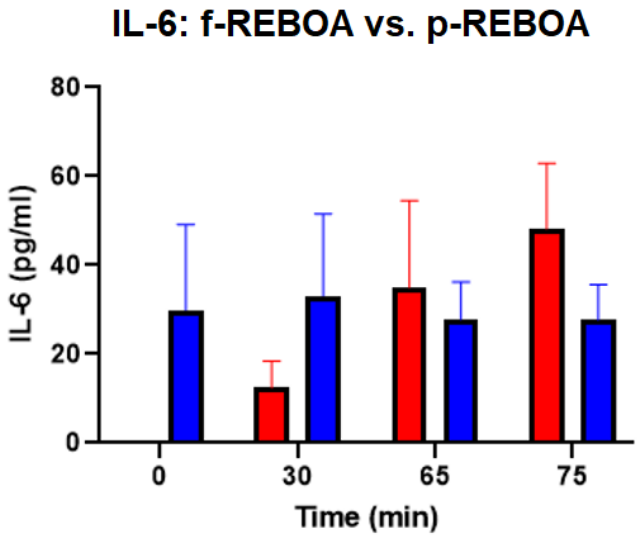
Figure 5. Syndecan-1 (SDC-1) levels over course of study differentiated by f-REBOA vs. p-REBOA

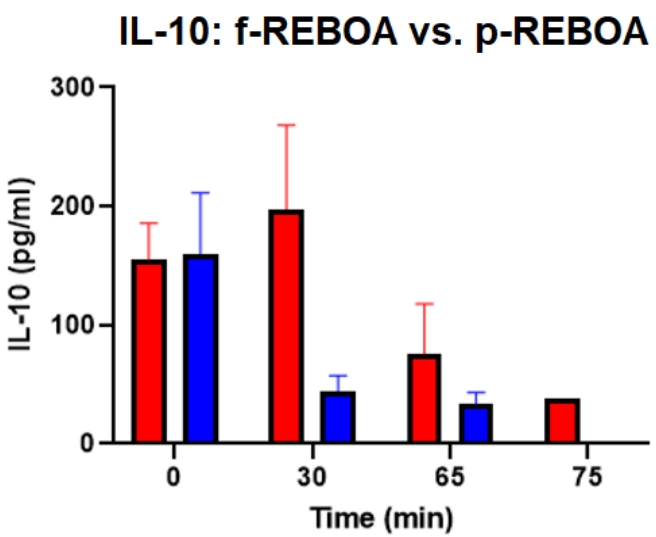
Additional Graphs and Figures

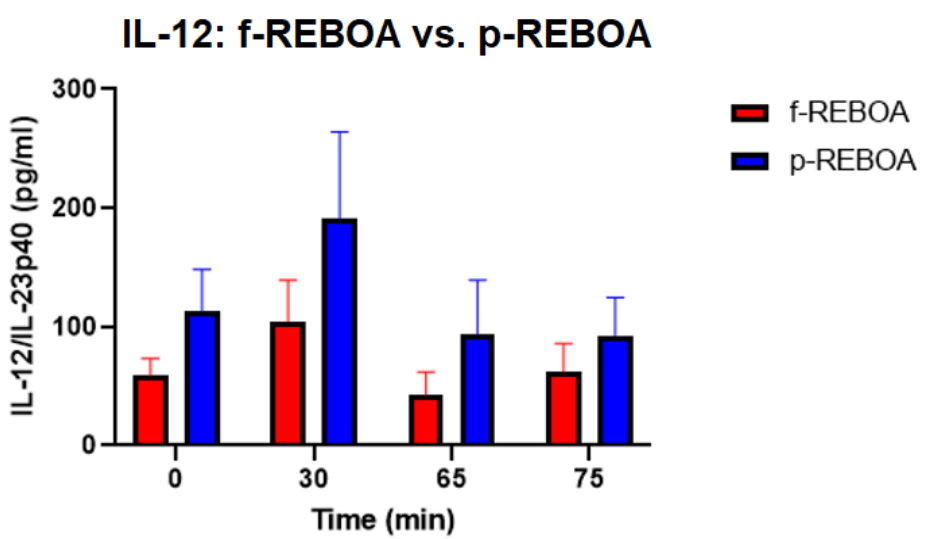
- Serum SDC-1 levels were not significantly different between groups ($p > 0.05$)
- Highest SDC-1 levels were observed at baseline, which may indicate natural variation between animals or effects of instrumentation
- Significant change over time ($p < 0.013$)

Results: Inflammatory Cytokines

- No significant difference in inflammatory markers between REBOA groups or time ($p > 0.05$)







Additional Graphs and Figures

Further investigations on **IL-10** and **IL-12** responses are needed.

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Conclusions

- Significant change over time for both HA and SDC-1 but not IL-6, IL-10, IL-12/IL-23p40
- No difference between occlusion type (p-REBOA vs. f-REBOA) for HA, SDC-1, or inflammatory cytokines
- T75 appears to be a critical timepoint, for at least HA, to consider extending study time course and increase sampling to characterize potential divergence between the p- vs. f-REBOA.
- Need to compare local tissue changes vs. systemic circulatory changes in HA.
- Future Directions
  - Further determine and characterize the relationship between REBOA-related altered hemodynamics & multiple additional endotheliopathy biomarkers, inflammatory cytokines, and components of coagulopathy.

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Questions?