

The Use of Lyophilized Plasma in a Severe Multi-injury Pig Model

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Background

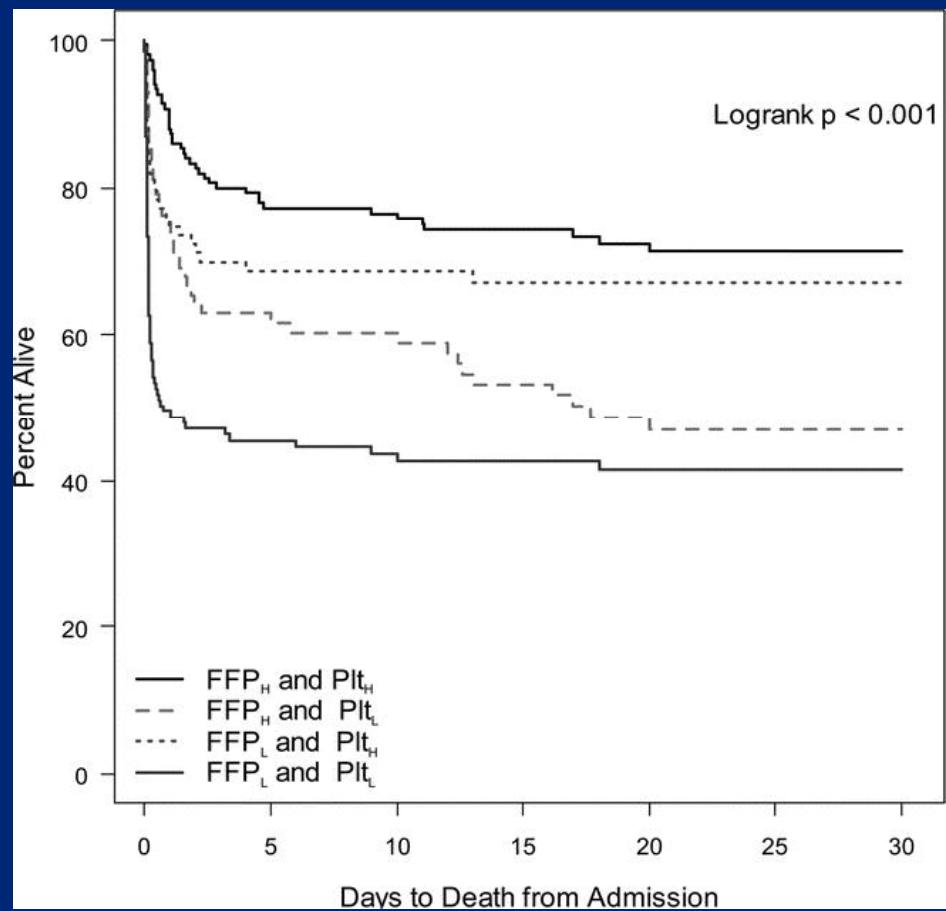
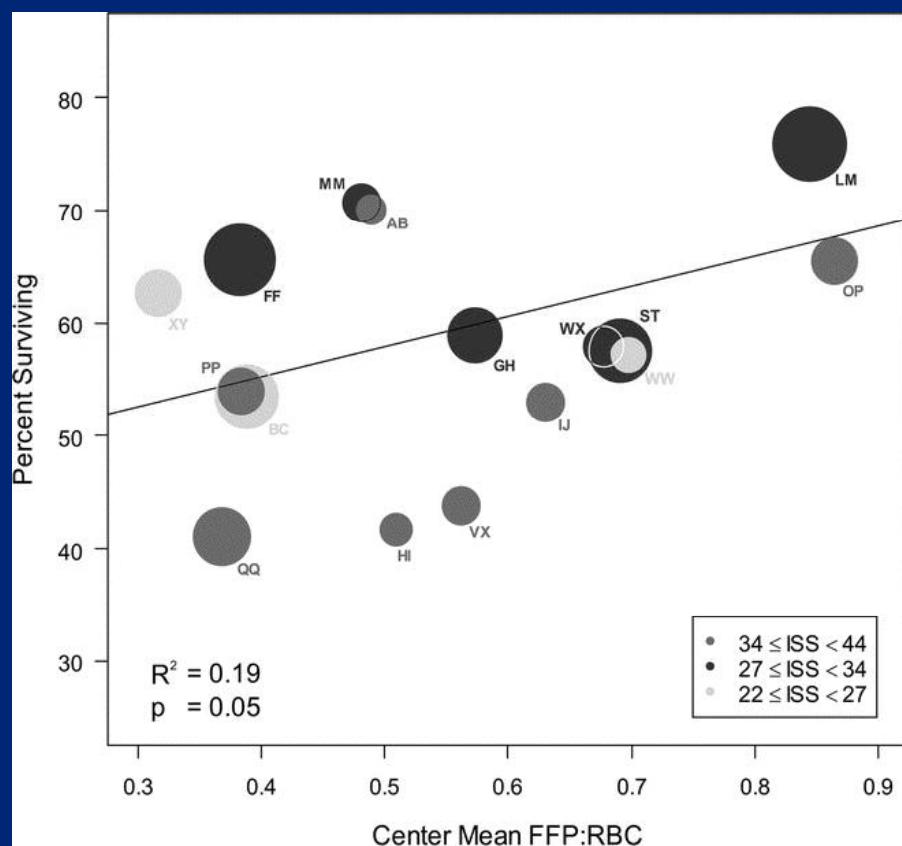
- Hemorrhage - leading cause of preventable death after trauma
- Acute coagulopathy of trauma - 25% of trauma patients
- High mortality in massively transfused



Hess, et al. *J Trauma* 2008
Brohi, et al. *Curr Opin Crit Care* 2007

Increased Plasma and Platelet to Red Blood Cell Ratios Improves Outcome in 466 Massively Transfused Civilian Trauma Patients

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The North Pacific Surgical Association

A high ratio of plasma and platelets to packed red blood cells in the first 6 hours of massive transfusion improves outcomes in a large multicenter study

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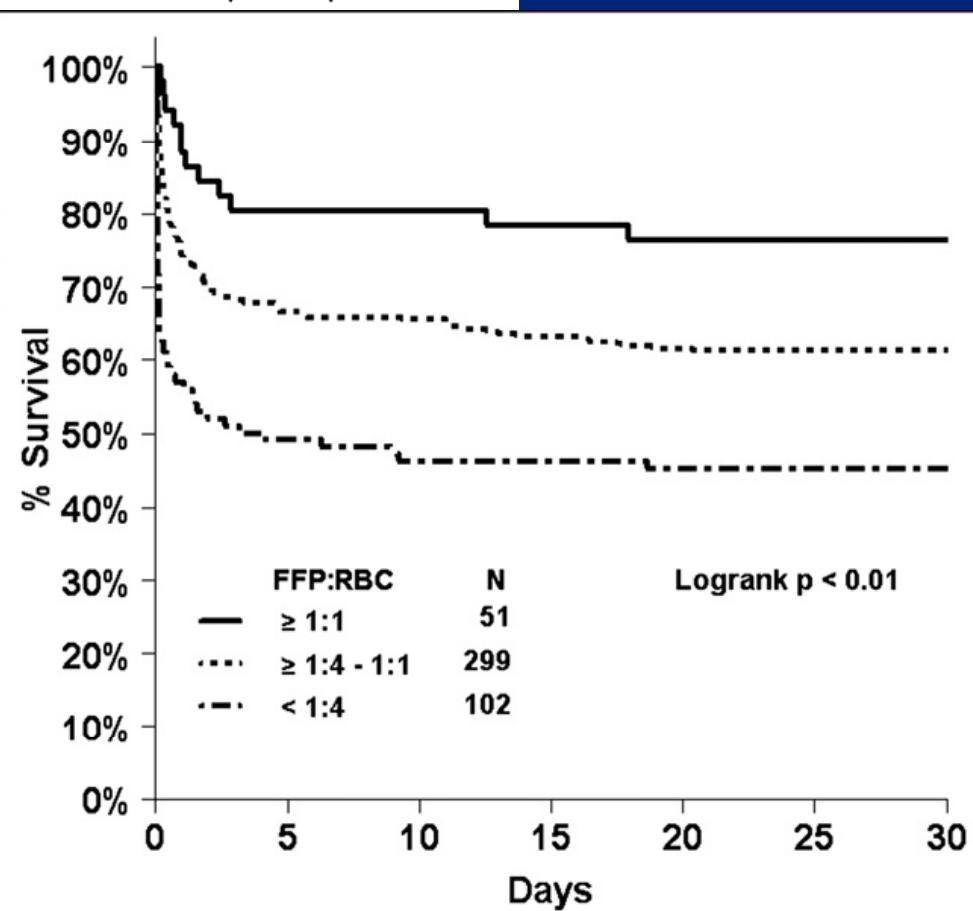
Table 3 Mortality differences and respiratory outcome based on the ratio of blood products

Product ratio	Measure	Transfusion ratio in first 6 hours				<i>P</i>
		<1:4	1:4-1:1	≥1:1		
FFP:PRBC	6 hour mortality %	37.3*	15.2*	2.0*	<0.001	
	In-hospital mortality %	54.9*	41.1*	25.5*	<0.04	
	Ventilator free days†	9	7.9	6.3	0.35	
PLT:PRBC	6 hour mortality %	22.8	19.0	3.2*	<0.002	
	In-hospital mortality %	43.7	46.8	27.4*	<0.03	
	Ventilator-free days†	6*	9.9**	9.1**	<0.004	

*Significant difference from other two ratios.

***P* = non-significant (0.79).

†Massive transfusion patients who survived >30 days (*n* = 277). Fisher exact test.



Joint Theater Trauma System

Clinical Practice Guideline

- “The goal in transfusion of the patient with need for massive transfusion is to deliver a ratio of PRBCs to plasma to platelets of 1:1:1”

High ratios problematic

- Plasma must be frozen
- Not immediately available
- Not available in far forward settings
- 1st availability in CSH
- Survival bias?

Objectives

- Evaluate the effect of lyophilization on factor activity
- Compare LP to FFP in a severe multi-system model
- Assess the effects of RBC's on coagulation

Methods

- Whole blood steriley removed from swine
- Plasma component separated
- Lyophilized by HemCon® Medical Technologies, Inc.
- Powdered plasma returned
- Reconstituted prior to transfusion



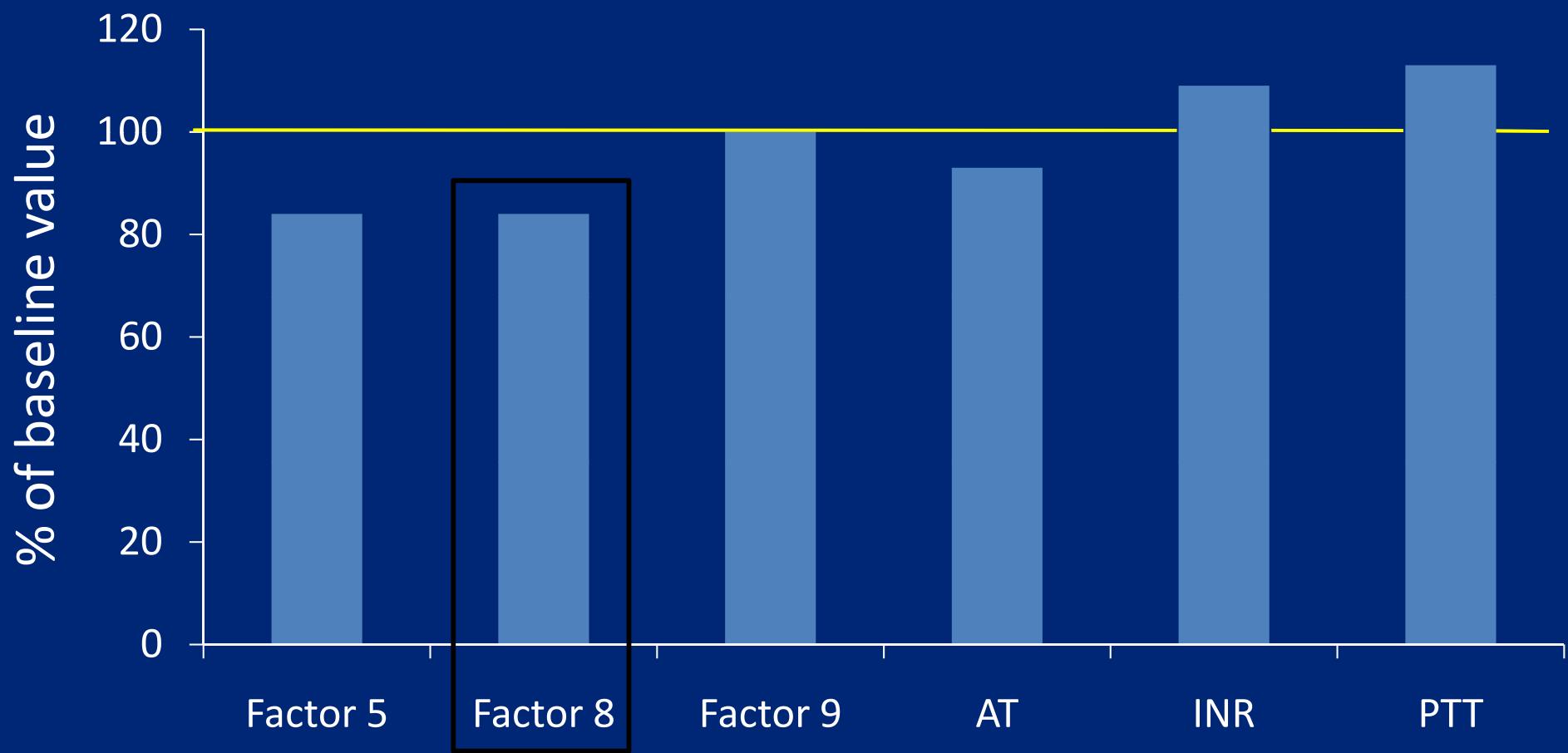
Methods

- LP very alkalotic
- Requires addition of acid to reconstitution fluid
- Vitamin C utilized
- Reconstitute to original volume

Methods

Clotting factor activity and coagulation parameters measured before lyophilization and after reconstitution

Residual Activity



Methods: Swine Model

- Multi - center trial
- OHSU, USAISR
- Previously validated model
- 32 Yorkshire crossbred swine
- Anesthetized, mechanically ventilated
- Carotid and jugular catheters placed

- Syverud et al, *Resuscitation* 1988
- Wladis et al, *Shock* 2001
- Kiraly et al, *J Trauma* 2006
- Cho et al, *Shock* 2008

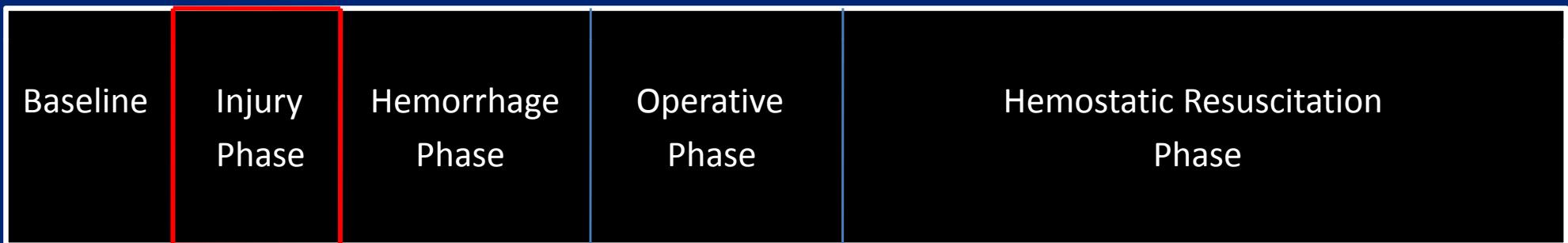




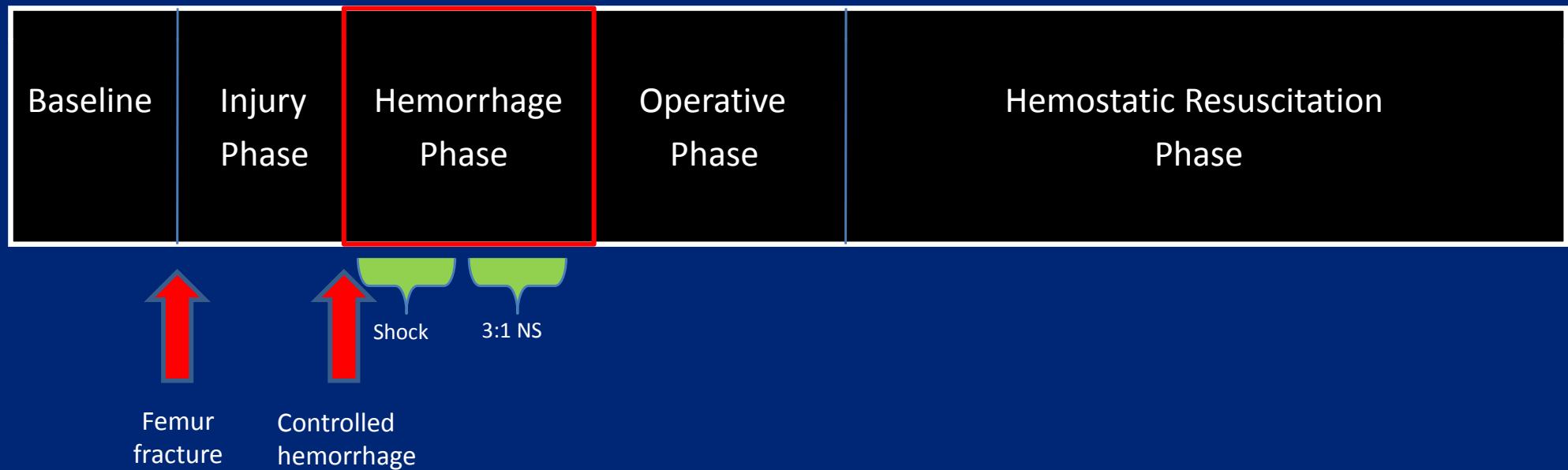
Cho, et al. *Shock* 2008

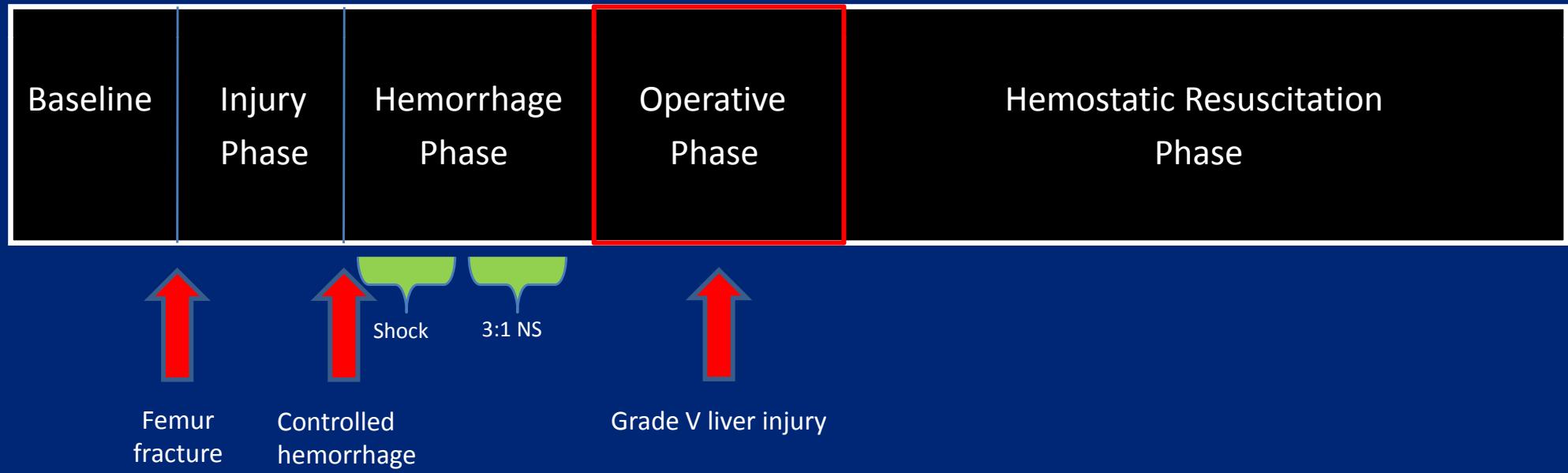
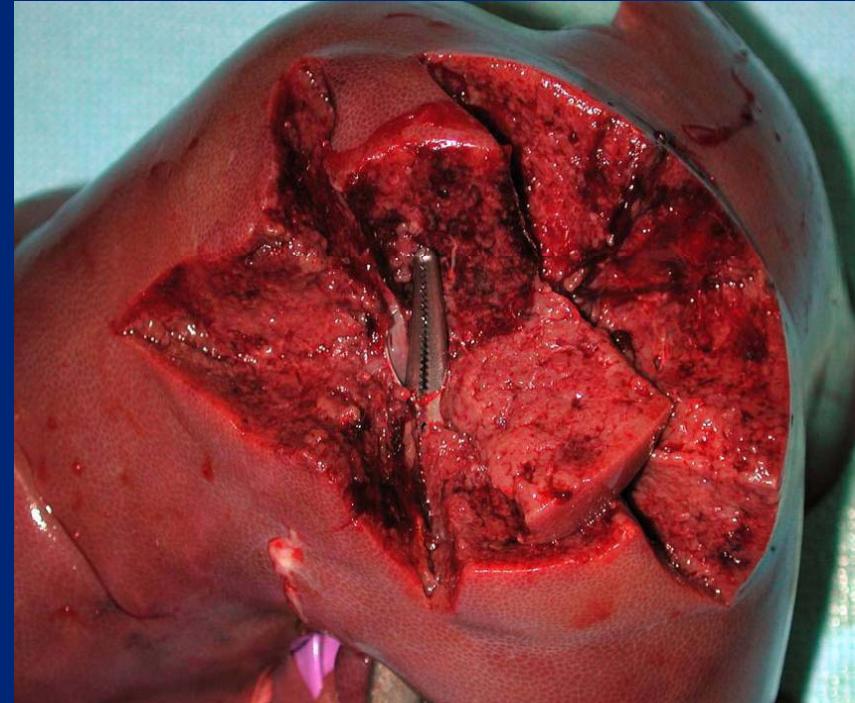
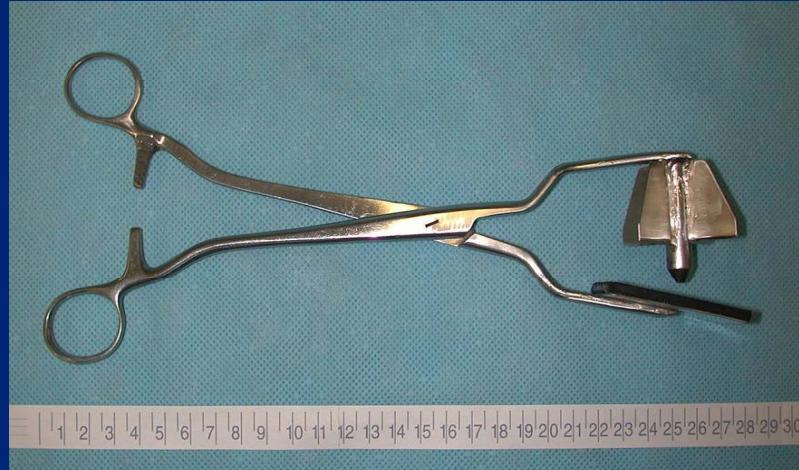


Shuja, et al, *J Trauma* 2008

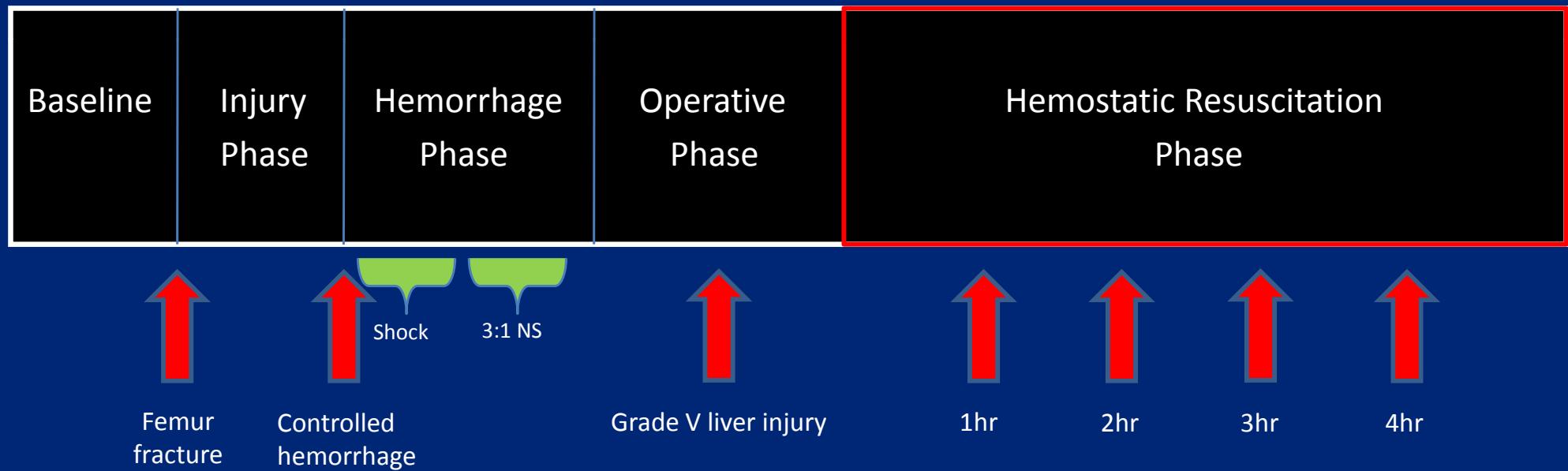


- 60% of estimated blood volume removed
- Hypothermia, acidosis, coagulopathy induced
 - Active cooling
 - Saline infusion

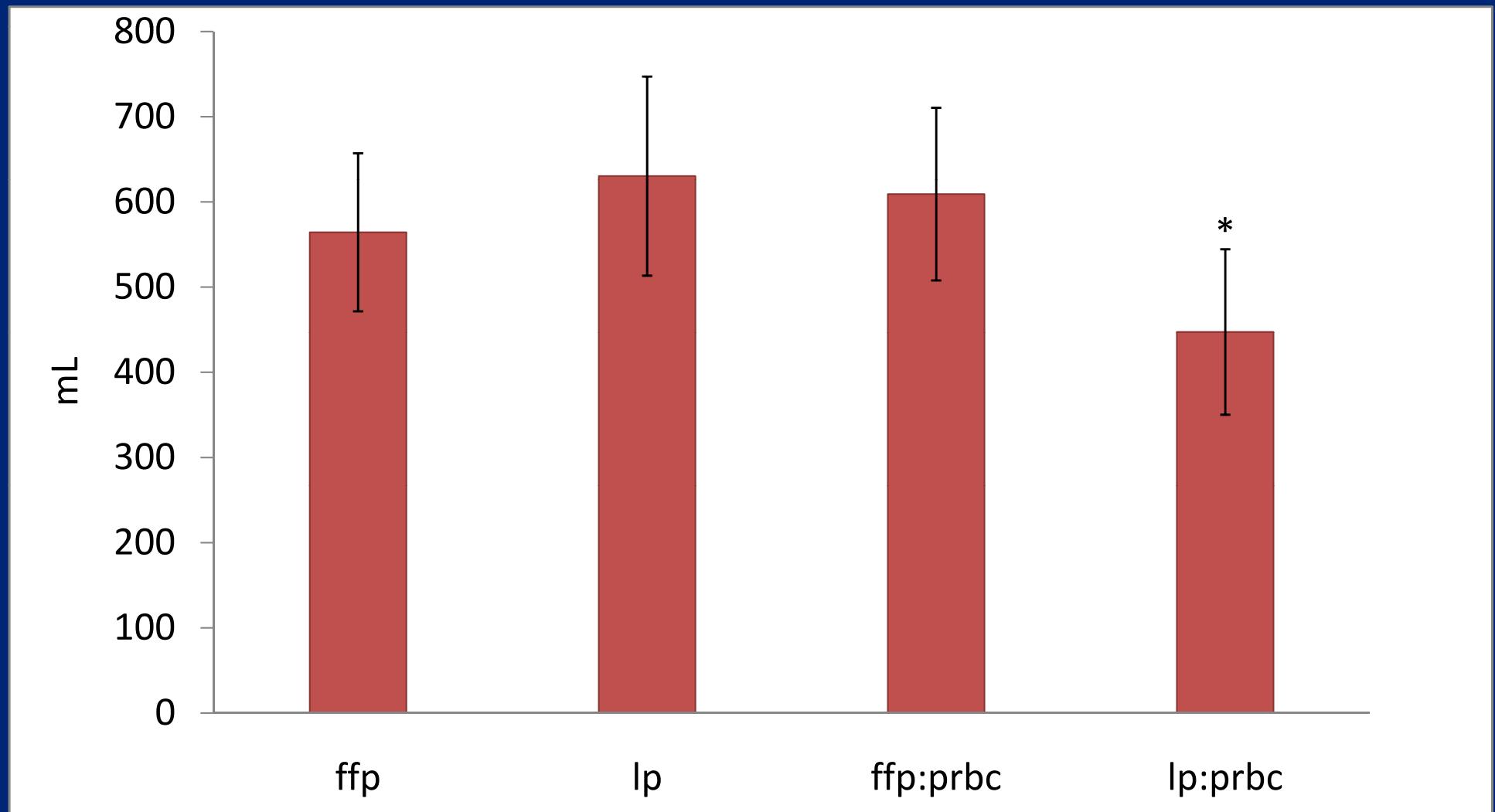




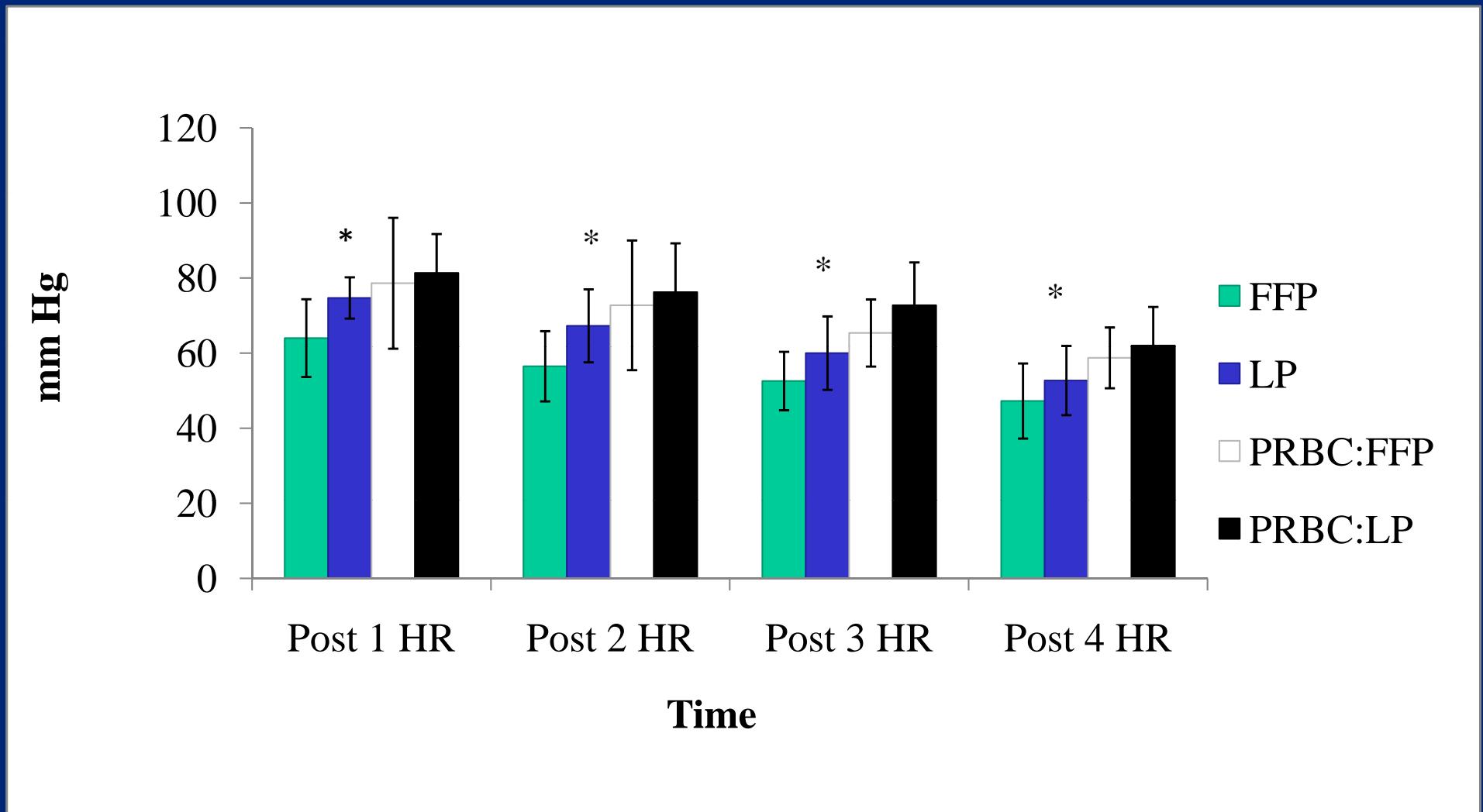
- 4 randomized groups
 - FFP
 - LP
 - FFP : PRBC
 - LP : PRBC
- Volume equal to controlled hemorrhage
- Re-warmed to 37°C
- Labs drawn hourly



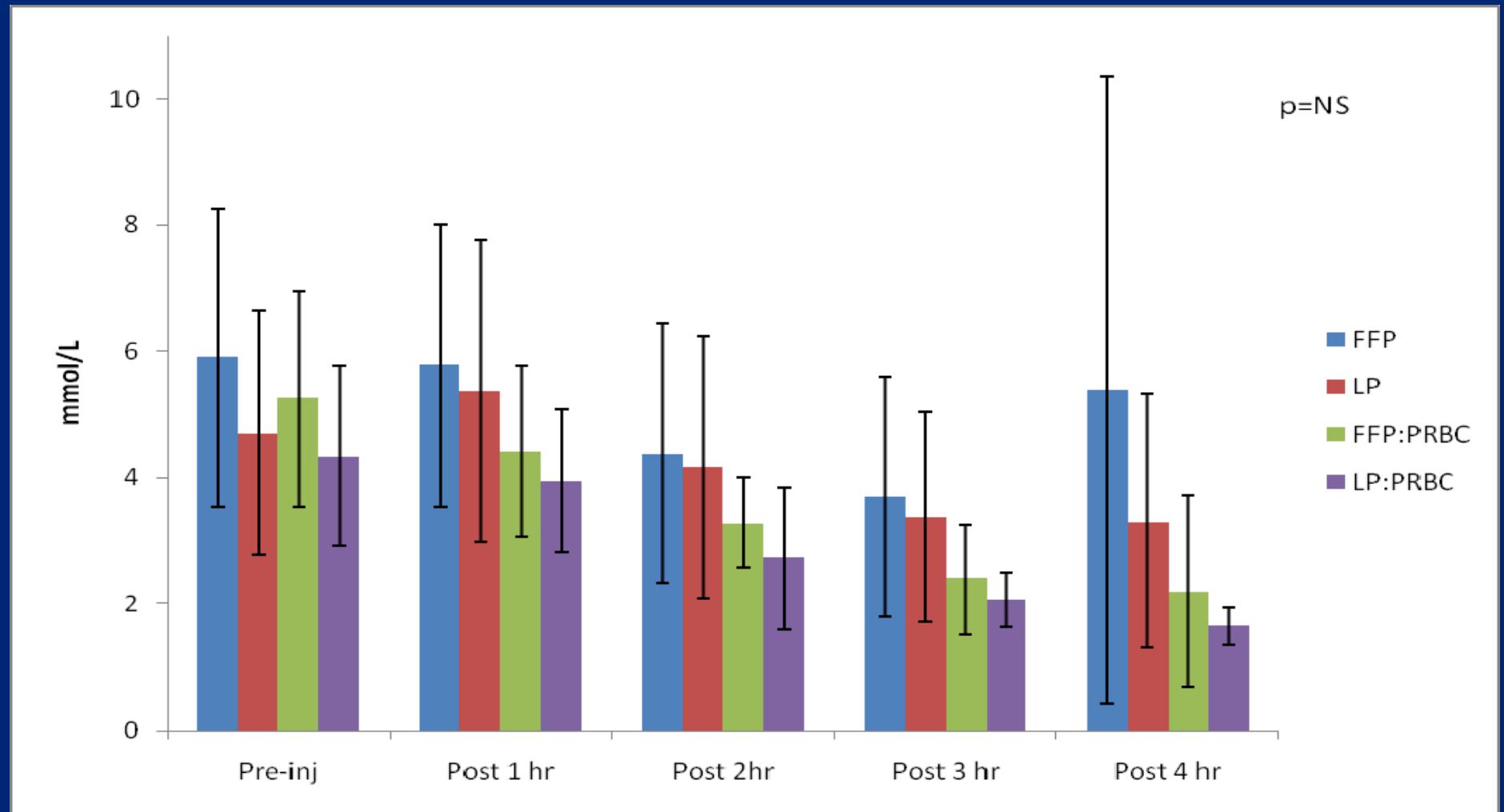
Blood loss after liver injury



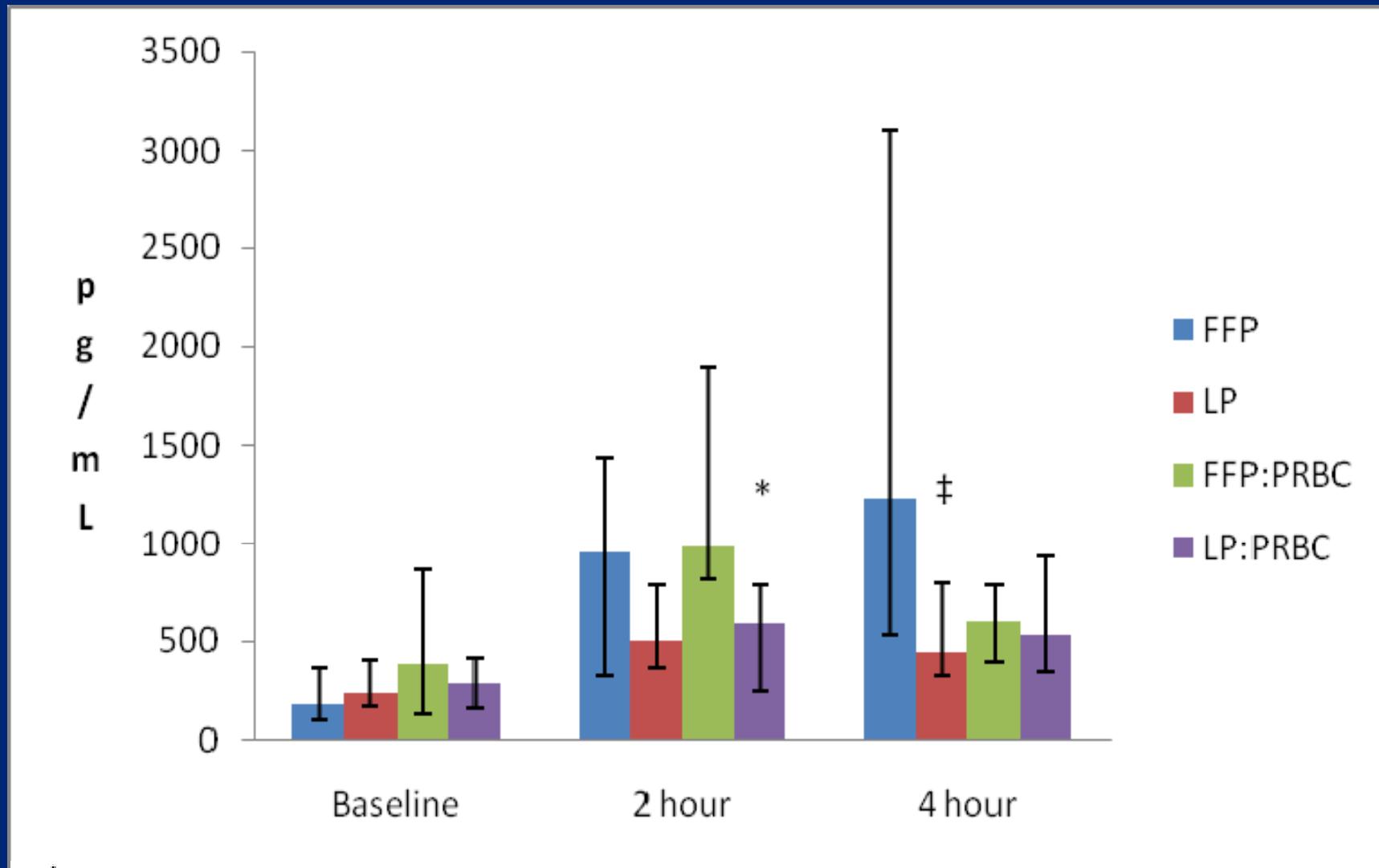
MAP



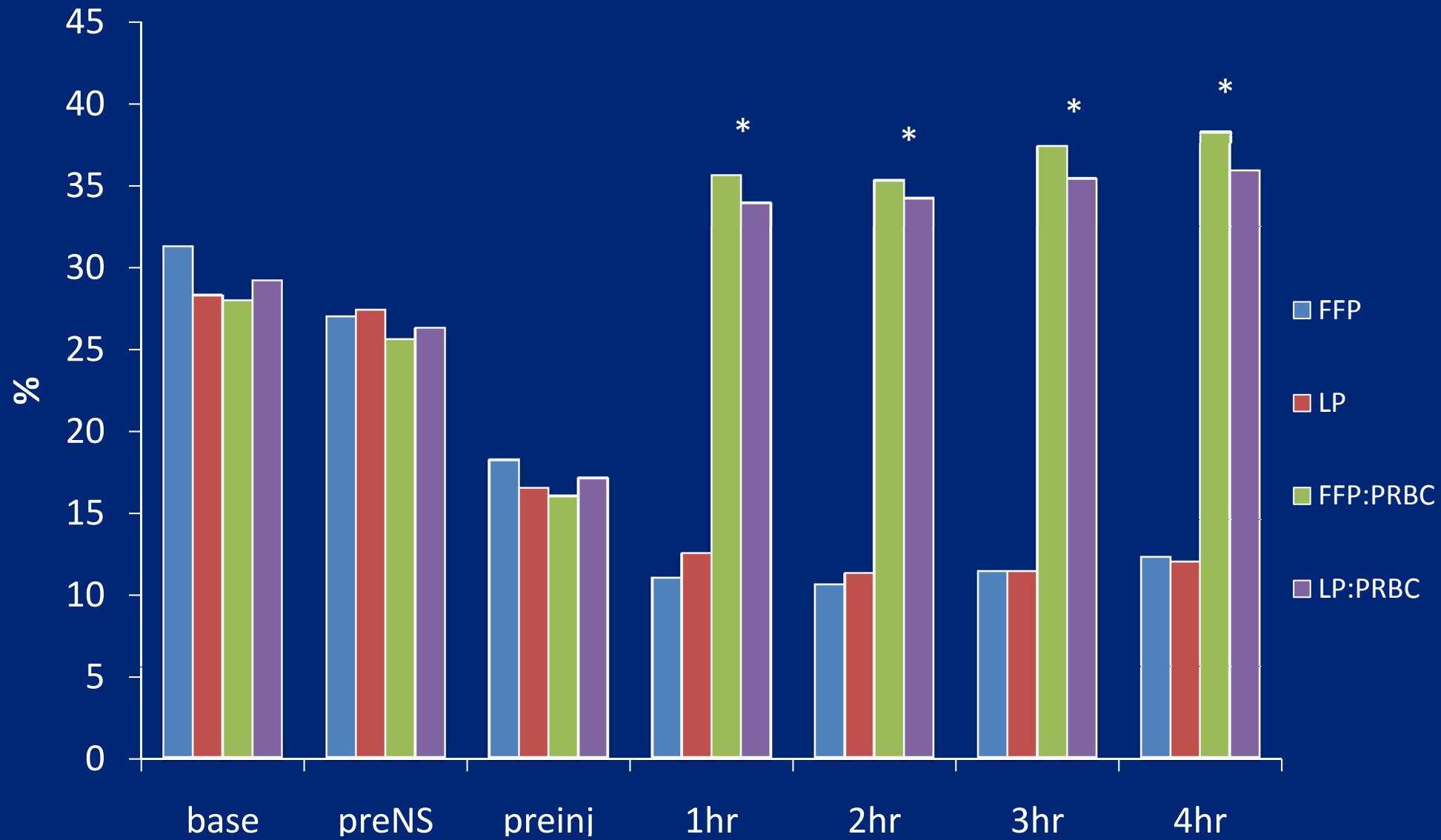
Lactate



IL-6

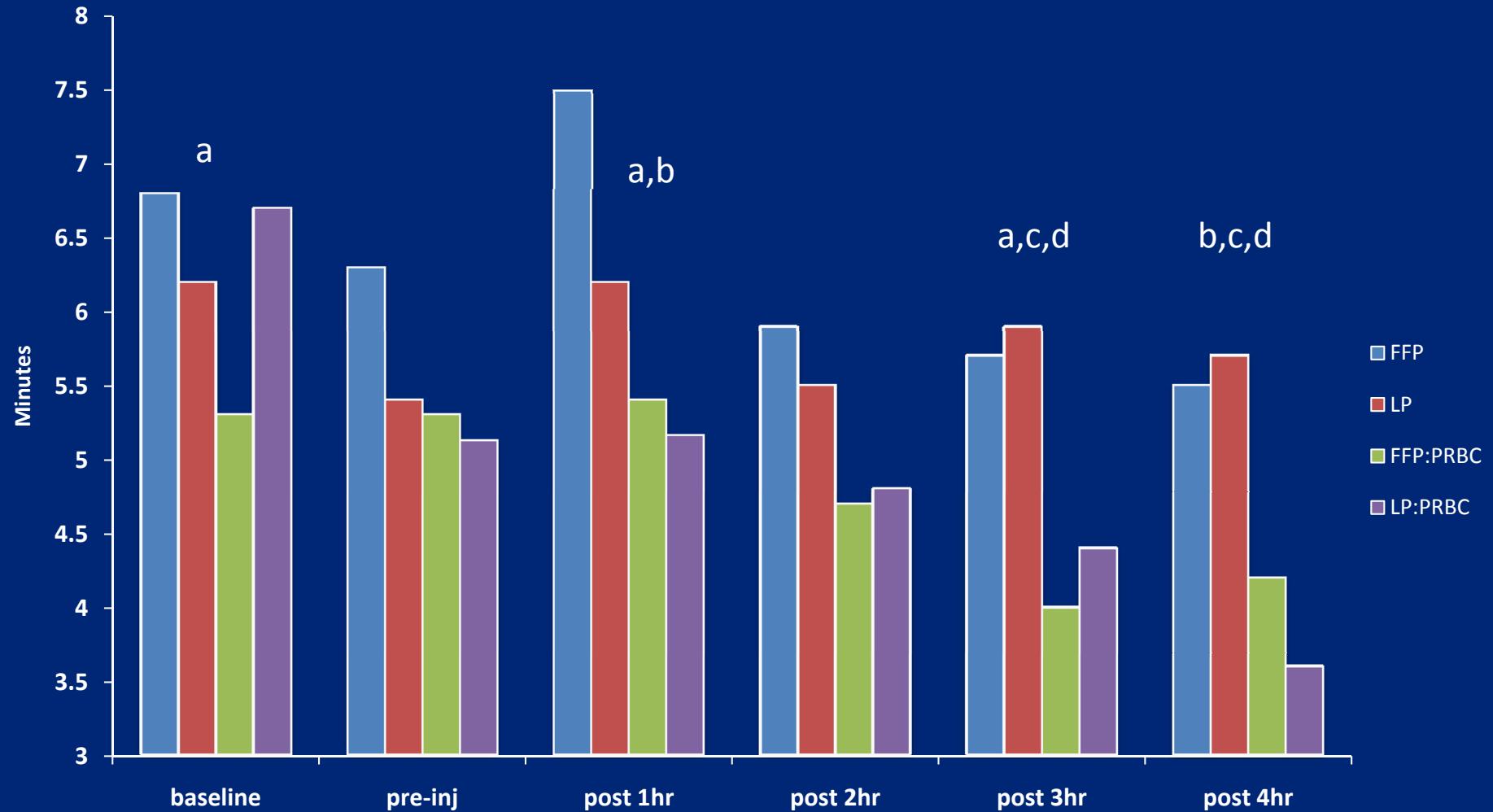


Hematocrit



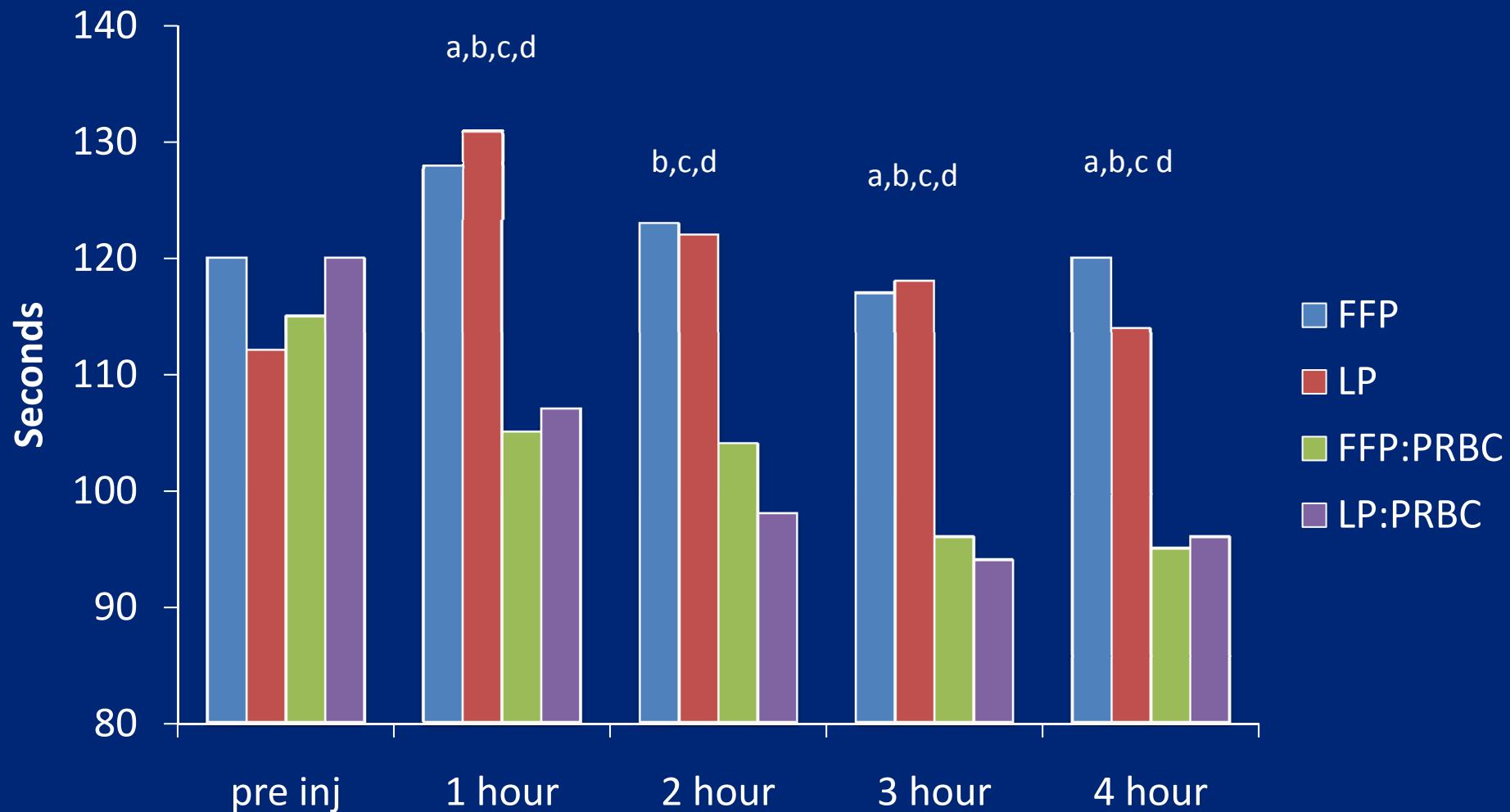
*p<0.001 comparing 1:1 groups to pure plasma groups

R time



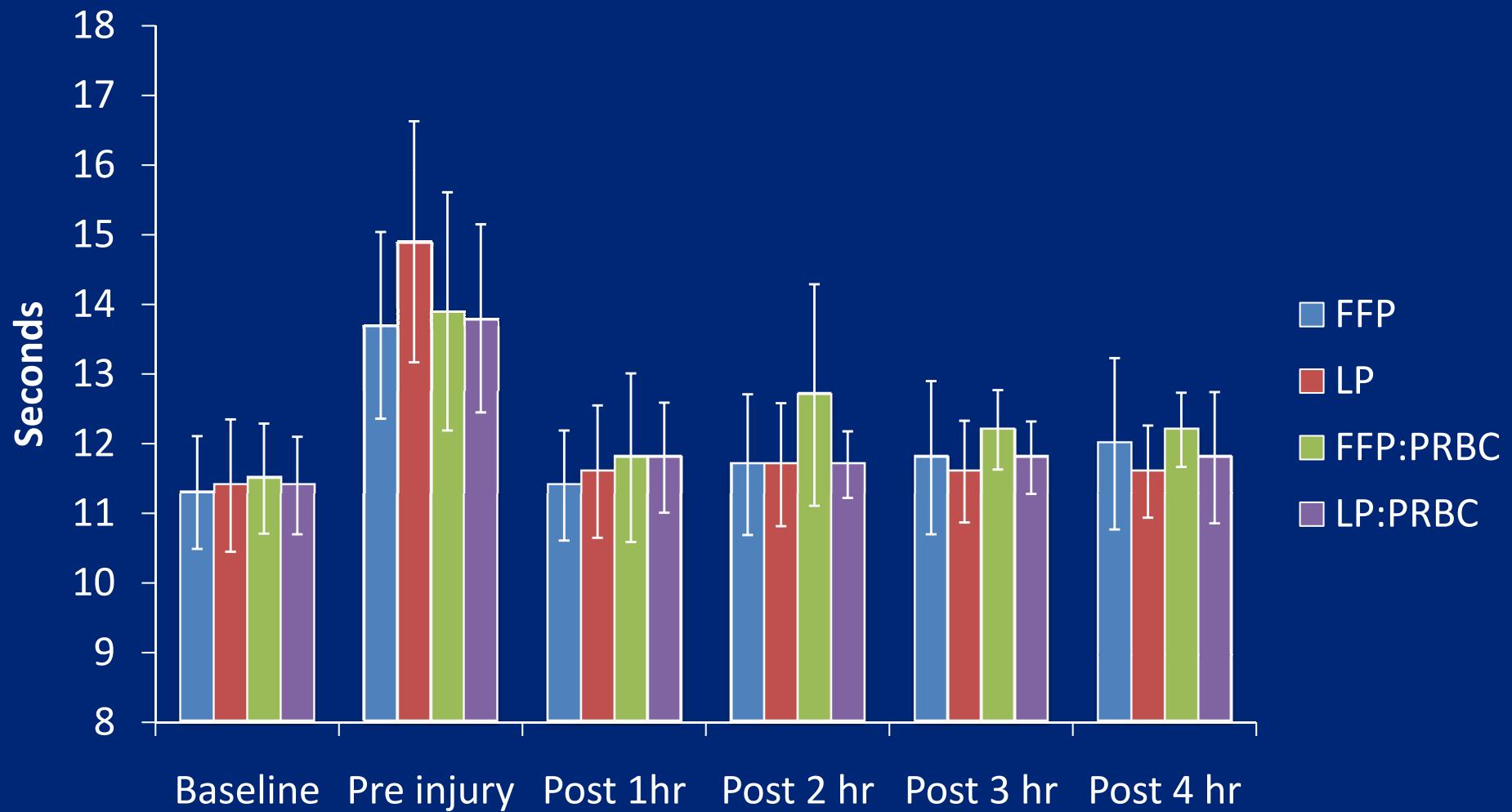
a=FFP greater than FFP:PRBC c=LP greater than FFP:PRBC
b=FFP greater than LP:PRBC d=LP greater than LP:PRBC

Activated Clotting Time



a= FFP:PRBC less than FFP c= LP:PRBC less than FFP
b=FFP:PRBC less than LP d=LP:PRBC less than LP

Prothrombin Time



Partial Thromboplastin Time

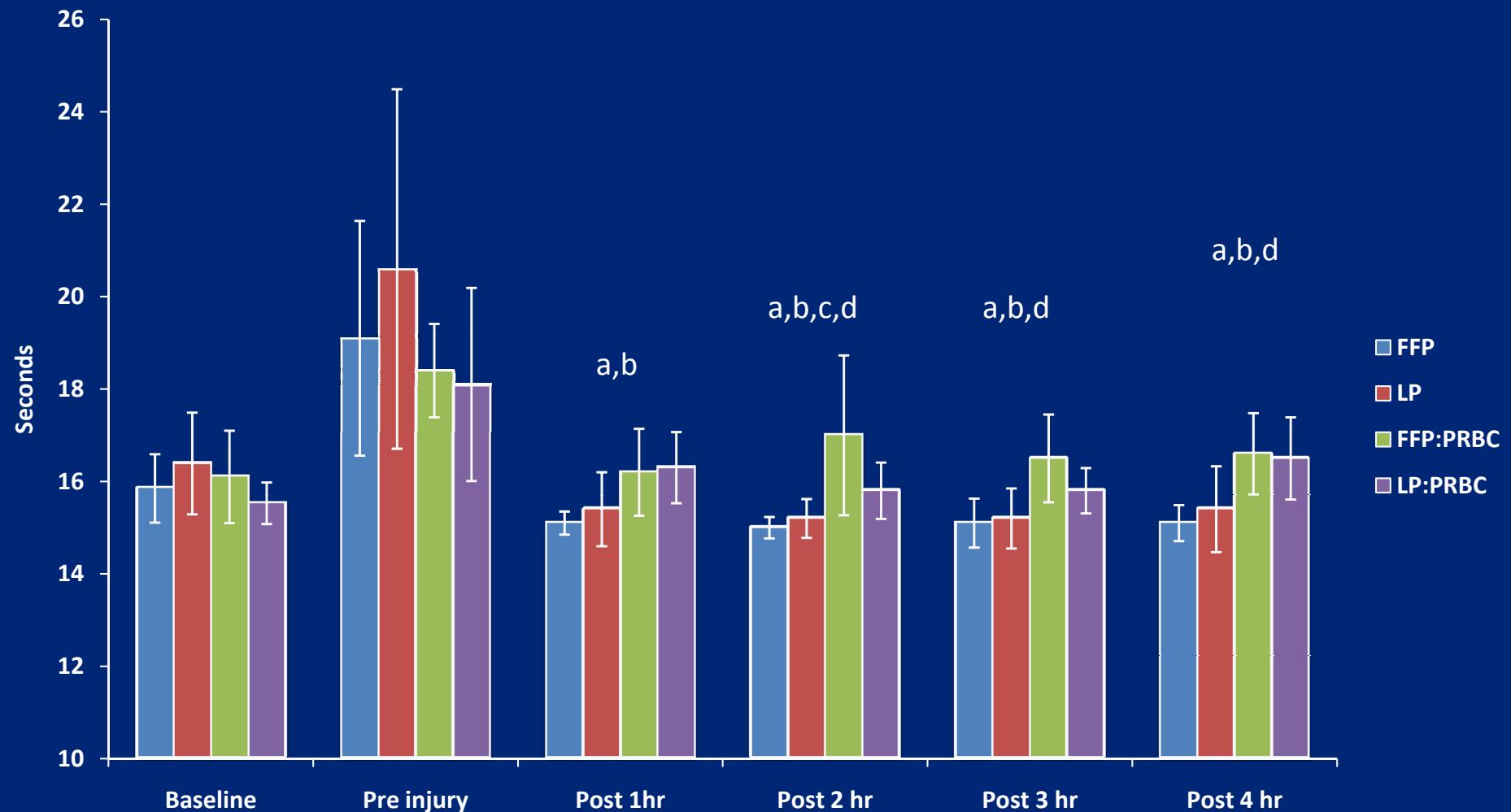
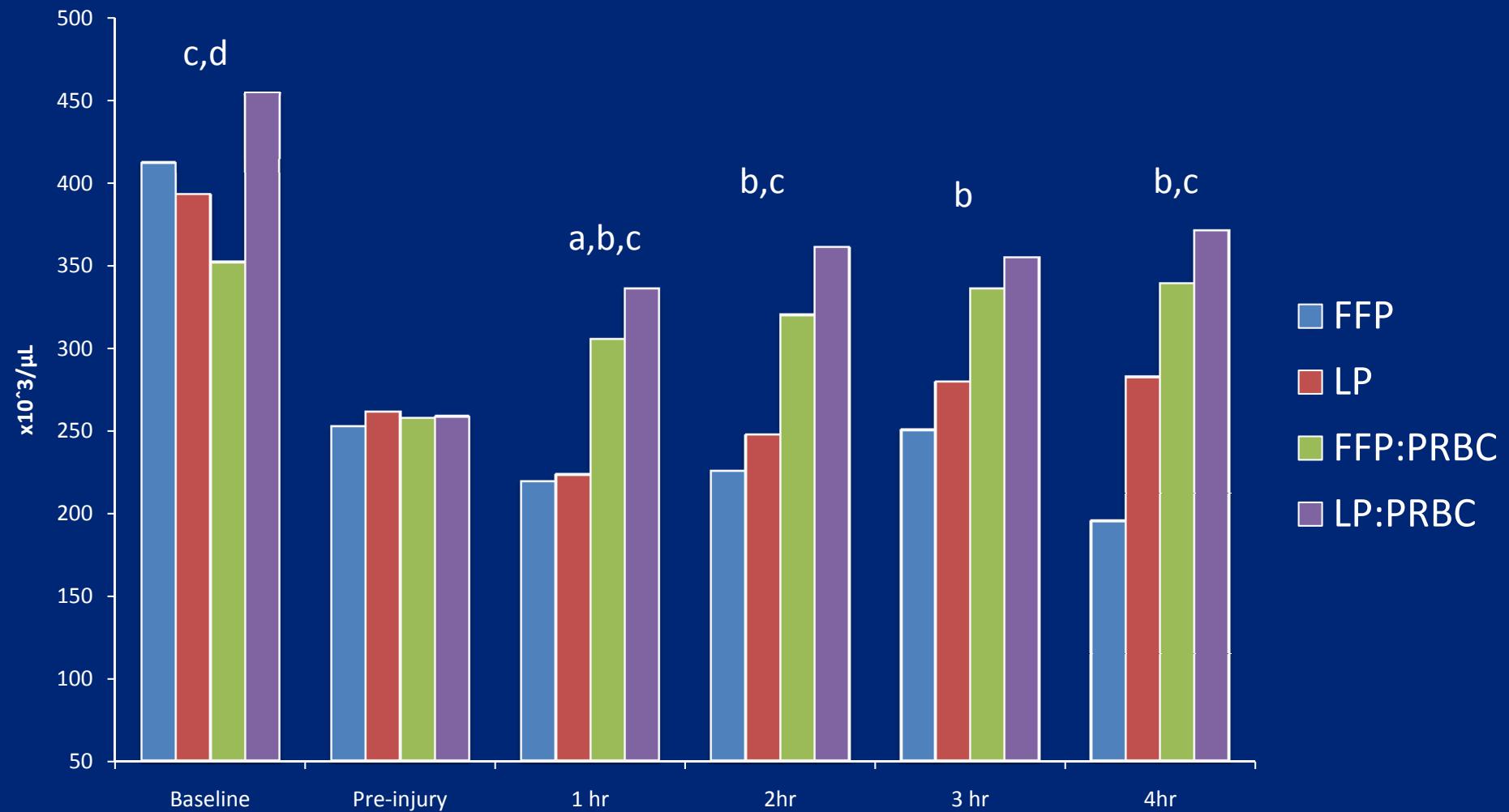
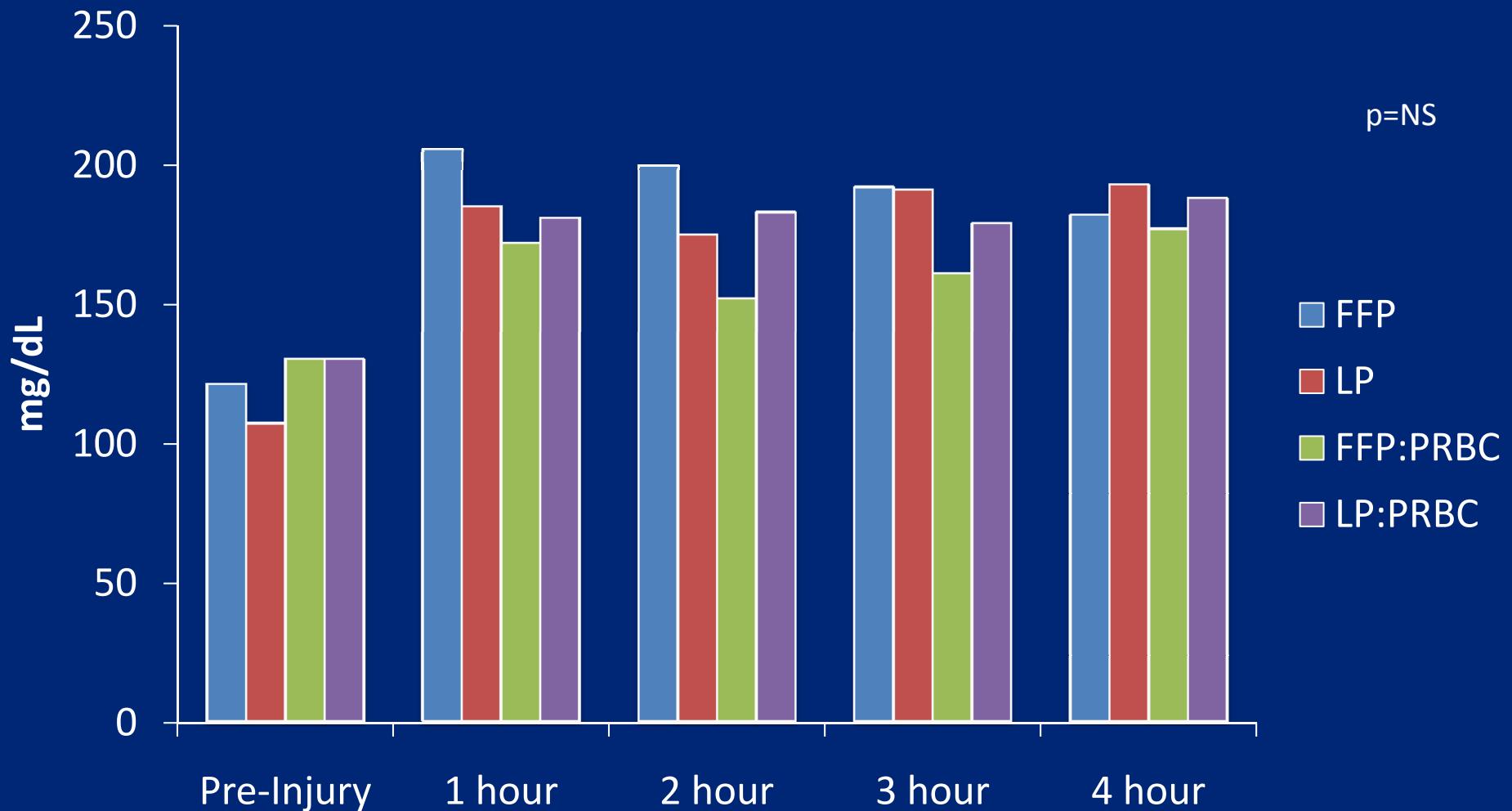


Figure 8. $p<0.05$ for comparisons a-d. a= FFP lower than LP:PRBC; b= FFP lower than FFP:PRBC; c=LP lower than LP:PRBC; d= LP lower than FFP:PRBC.

Platelet Count



Fibrinogen



Discussion

- Decreased blood loss LP:PRBC group
 - LP retains coagulation factor activity
 - RBC affects
- Accelerated coagulation in PRBC groups
 - Add pure PRBC group
 - TEG vs standard coag assays
- Decreased inflammation in LP group
 - Vitamin C?

Mechanisms

- RBC crucial participant in clot – cell membrane, phospholipids



Mechanisms

- RBC contribute to biomechanical margination of platelets
 - Rouleaux formation
 - Enhance concentration of plt near endothelium
- RBCs modulate platelet production of thromboxane

Future Studies

- Citrate vs HCl vs Vitamin C
- Minimize volume of reconstitution fluid
- Optimize type of reconstitution fluid
- Study additional anti-oxidants
- Survival studies with optimized fluid

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