Leukoreduction of Whole Blood with Platelet Sparing Filter

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Disclosures

- Consultant
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  - Norwegian Navy Blood Research Program
  - Instrumentation Labs
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- Research Support
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To Filter or Not to Filter WB

Is this a life or death ?

Imuflex-SP filter

- Approved leukoreduction filter for whole blood that is platelet sparing
  - Number not function
- In use at many trauma centers and blood suppliers
  - 50% of LTOWB programs

Leukoreduction Benefits

- Reduced CMV transmission
- Reduced alloimmunization
- Reduced fever
- Clinical Outcome Benefits?
  - Mortality, organ failure, infection?

Journal of Surgical Research **138,** 32–36 (2007)
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Association for Academic Surgery, 2006

Leukoreduction Before Red Blood Cell Transfusion Has No Impact on Mortality in Trauma Patients[1]

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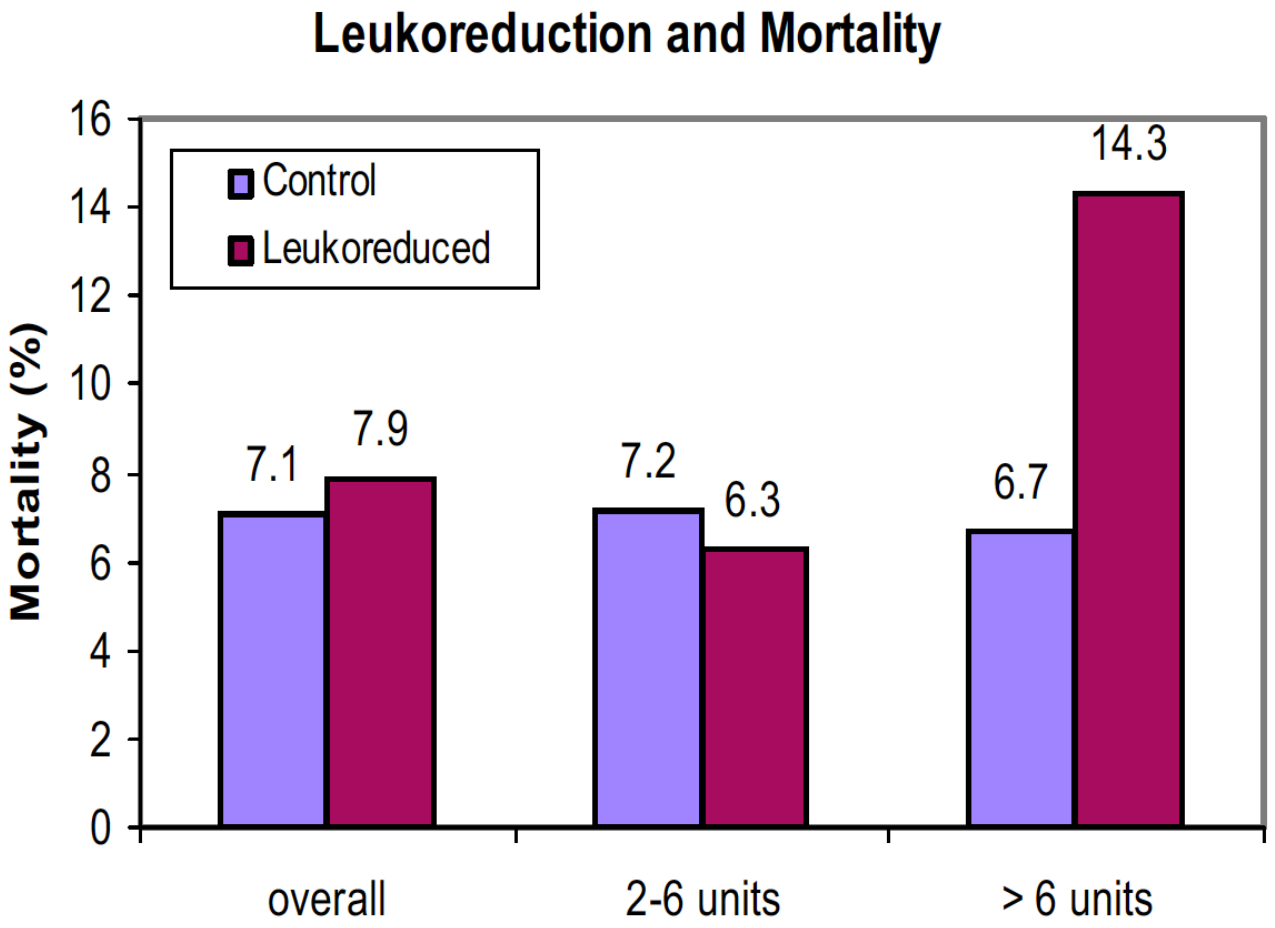
Patient Characteristics

	Overall			Massive transfusion		
	Control $n = 439$	Intervention (leukoreduced) $n = 240$	P-value	Control $n = 119$	Intervention (leukoreduced) $n = 49$	P-value
Age (mean ± SD)	39.4 ± 18.8	39.8 ± 19.0	0.82	36.3 ± 15.6	36.6 ± 16.4	0.92
ISS (mean ± SD)	21.6 ± 12.6	19.5 ± 11.8	0.03	25.1 ± 12.5	21.3 ± 12.1	0.07
Units of RBC in first 24 h (median ± IQR)	4 ± 6	3 ± 4	0.82	11 ± 9	10 ± 7	0.34
Male	73.8%	66.3%	0.05	78.2%	73.5%	0.51
Blunt	76.5%	73.8%	0.48	67.2%	57.1%	0.22
Penetrating	23.5%	26.3%	0.48	32.8%	42.9%	0.22

SD, standard deviation; ISS, Injury Severity Score; RBC, red blood cells; IQR, interquartile range.


Leukoreduction and Mortality
Mortality (%)
16
14
12
10
8
6
4
2
0
Control
Leukoreduced
7.1
7.9
7.2
6.3
6.7
14.3
overall
2-6 units
> 6 units

The use of leukoreduced red blood cell products is associated with fewer infectious complications in trauma patients

The American Journal of Surgery (2008) 196, 56–61

Randall S. Friese, M.D.[a,*], Jason L. Sperry, M.D.[b], Herb A. Phelan, M.D.[a], Larry M. Gentilello, M.D.[a]

[a]Division of Burn, Trauma, Critical Care, Department of Surgery, University of Texas Southwestern Medical Center at Dallas, Dallas, TX, USA; [b]Division of Trauma and General Surgery, Department of Surgery, University of Pittsburgh Medical Center, Pittsburgh, PA, USA

Table 1 Overall patient characteristics (n = 678)

Variable	Control group (n = 438)	Leukoreduction group (n = 240)	*P*
Age in years (mean ± SD)	39.4 ± 18.8	39.8 ± 19.0	.82
ISS (median [IQR])	20 [10, 29]	17 [9.25, 25.75]	.02
Units of RBC in first 24 hours (median [IQR])	4 [2, 8]	3 [2, 6]	.01
Male (%)	73.8	66.3	.05
Blunt (%)	76.5	73.8	.48
Penetrating trauma (%)	23.5	26.3	.48
Ventilator days (mean ± SD)	6.64 ± 10.5	4.74 ± 8.93	.04

LOS = length of stay; IQR = interquartile range.

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Table 3 Regression analysis (odds for pneumonia)

Variable	Overall group (95% CI)[a]	Massive-transfusion subset (95% CI)[b]
Age (y) in years	1.003 (.991–1.016)	1.018 (.995–1.042)
ISS (17–24)[c]	2.610 (1.223–5.567)	4.998 (1.342–18.61)
ISS (>25)[c]	6.437 (3.303–12.55)	8.428 (2.616–27.15)
Head and neck AIS (4–6)	1.992 (1.197–3.315)	1.705 (.645–4.505)
Units RBCs	1.064 (1.033–1.096)	N/A
Sex (male)	1.151 (.693–1.912)	1.209 (.502–2.913)
LR RBCs	.545 (.329–.905)	.292 (.113–.756)
Mechanism (blunt)	1.692 (.884–3.241)	1.203 (.498–2.905)
Hosmer-Lemeshow goodness-of-fit	.972	.565

RBC = red blood cell; LR = leukoreduced.
[a]n = 678; [b]n = 168; [c]reference ISS 1 to 16.

Table 4 Regression analysis (odds for any infection)

Variable	Overall group (95% CI)[a]	Massive-transfusion subset (95% CI)[b]
Age (y)	1.002 (.991–1.012)	1.018 (.996–1.041)
ISS (17–24)[c]	2.713 (1.567–4.697)	2.495 (.885–7.030)
ISS (>25)[c]	4.535 (2.733–7.526)	5.835 (2.390–14.25)
Head and neck AIS (4–6)	1.655 (1.035–2.647)	1.037 (.390–2.759)
Units RBCs	1.067 (1.036–1.098)	N/A
Sex (male)	1.240 (.802–1.917)	1.028 (.451–2.344)
LR RBCs	.479 (.314–.730)	.326 (.145–.730)
Mechanism (blunt)	1.442 (.864–2.409)	1.429 (.653–3.126)
Hosmer-Lemeshow goodness-of-fit	.492	.231

RBC = red blood cell; LR = leukoreduced.
[a]n = 678; [b]n = 168; [c]reference ISS 1 to 16.

SHOCK, Vol. 26, No. 4, pp. 342–347, 2006

THE EFFECTS OF LEUKOREDUCED BLOOD TRANSFUSION ON INFECTION RISK FOLLOWING INJURY: A RANDOMIZED CONTROLLED TRIAL

Avery B. Nathens,* Theresa A. Nester,†‡ Gordon D. Rubenfeld,§ Raminder Nirula,¶ and Terry B. Gernsheimer†§

**Department of Surgery and the Harborview Injury Prevention and Research Center, †Puget Sound Blood Center, ‡Department of Laboratory Medicine, and §Department of Medicine, University of Washington, Seattle, WA; and ¶Department of Surgery, Medical College of Wisconsin, Milwaukee, WI*

TABLE 3. **Infectious complications in evaluable subjects***

	Standard (n = 136)	Leukoreduced (n = 132)	RR (95% CI)
Pneumonia			
All diagnoses	16 (12)	13 (10)	0.84 (0.40–1.8)
Invasive diagnosis only†	8 (5.9)	8 (6.1)	1.03 (0.39–2.7)
Bloodstream infections	4 (2.9)	5 (3.5)	1.29 (0.35–4.8)
Surgical site infections	22 (16)	17 (13)	0.80 (0.42–1.5)
Urinary tract infections	21 (15)	14 (11)	0.69 (0.35–1.4)
Pseudomembranous colitis	4 (3.0)	0	NA
Any infection	49 (36)	40 (30)	0.84 (0.55–1.3)

*Values in parentheses represent percent of patients.
†Diagnosis obtained by bronchoscopic alveolar lavage.
CI indicates confidence interval; NA, not applicable.

TABLE 5. **Secondary end points in evaluable subjects***

	Standard	Leukoreduced	RR (95% CI)
Fever days (per 100 days at risk)	19.9	19.7	1.01 (0.89–1.2)
Mortality (n [%])			
Hospital	27 (20)	29 (22)	1.16 (0.72–1.9)
28-day	26 (19)	29 (22)	1.20 (0.74–1.9)
28-day (intent-to-treat population)	26 (15)	29 (19)	1.19 (0.73–1.9)
	Standard	Leukoreduced	*P*
Median length of stay (interquartile range)			
Hospital	13.0 (6–25)	12.5 (6–21)	0.49
ICU	3 (0.7–11)	4 (1–10)	0.59
Median ventilator days (interquartile range)	2.5 (1–10)	3 (1–8.5)	0.90
Mean Marshall MOD score (SD)	5.9 (4.9)	6.6 (5.7)	0.26

*Except where specified under 28-day mortality in which all patients who were randomized and met inclusion criteria were available for analysis. ICU indicates intensive care unit; MOD, multiple organ dysfunction. Some abbreviations are explained in the footnote to Table 3.

Effects of leukoreduced blood on acute lung injury after trauma: A randomized controlled trial*

Crit Care Med 2008 Vol. 36, No. 5

Timothy R. Watkins, MD; Gordon D. Rubenfeld, MD, MSc; Thomas R. Martin, MD; Theresa A. Nester, MD; Ellen Caldwell, MS; Jens Billgren; John Ruzinski; Avery B. Nathens, MD, PhD

Table 3. Lung injury outcomes

	Standard N = 136	Leukoreduced N = 132	RR	95% Confidence Interval
Early (≤72 hours from injury)				
ALI	31 (23)	32 (24)	1.06	(.69, 1.64)
ARDS	15 (11)	14 (11)	.96	(.48, 1.91)
Late (>72 hours from injury)				
ALI	28 (21)	24 (18)	.88	(.54, 1.44)
ARDS	26 (19)	24 (18)	.95	(.58, 1.57)
Hospital course (28 day)				
Requirement for mechanical ventilation	106 (78)	103 (78)	1.00	(.88, 1.14)
Hospital day of ALI diagnosis[a]	3 (2, 6)	3 (2, 5)	$p = .6974$	
Number of ventilator-free days[b]	18 (11)	18 (11)	$p = .8892$	95% CI (−2.87, 2.49)

Effects of allogeneic leukocytes in blood transfusions during cardiac surgery on inflammatory mediators and postoperative complications*

Crit Care Med 2010 Vol. 38, No. 2

Yavuz M. Bilgin, MD; Leo M. G. van de Watering, MD, PhD; Michel I. M. Versteegh, MD; Marinus H. J. van Oers, MD, PhD; Anneke Brand, MD, PhD

Table 4. Multivariate analyses of risk factors associated with postoperative complications

	All Postoperative Complications OR (95% CI)	*p*	Infections OR (95% CI)	*p*	MODS OR (95% CI)	*p*	Hospital Mortality OR (95% CI)	*p*
Parsonnet score	1.18 (0.95–1.46)	.13	1.16 (0.92–1.47)	.20	0.98 (0.76–1.31)	.98	1.70 (1.04–2.78)	.04
Gender							2.09 (0.70–6.22)	.19
Randomization arm	1.46 (0.87–2.49)	.15	2.01 (1.15–3.54)	.01			1.92 (0.67–5.51)	.22

Consequences of LR – Platelet Sparing Filter

- Reduction in hemostatic potential ?

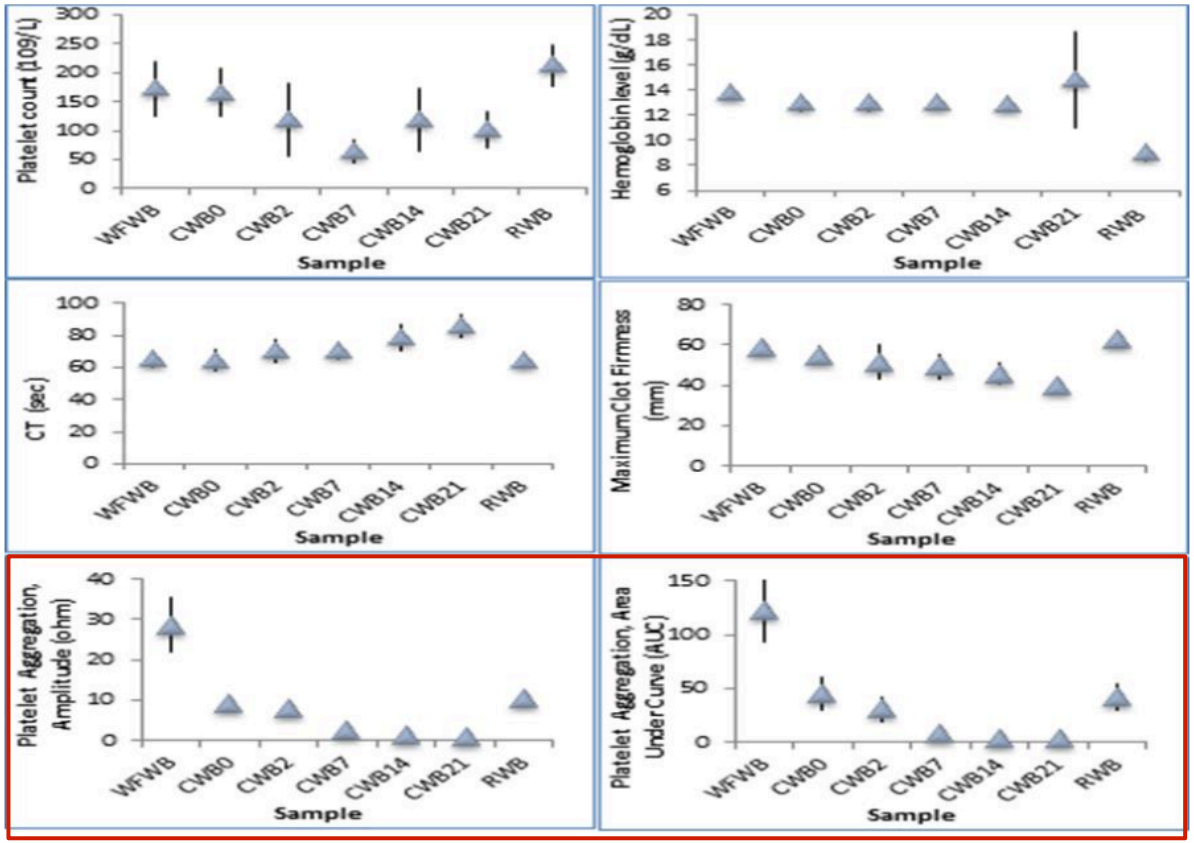
Journal of Thrombosis and Circulation Open Access

Zielinski et al., J Thrombo Cir 2018, 4:1
DOI: 10.4172/2572-9462.1000124

Research Article Open Access

In vitro Analysis of the Hemostatic Properties of Whole Blood Products Prepared with a Platelet-Sparing Leukoreduction Filter

Zielinski MD[1*], Stubbs JR[2], Polites SF[1], Xue A[3], Haugen DAL[4], Emery R[2], Jenkins DH[5] and Park MS[1]



Preparation of leukoreduced whole blood for transfusion in austere environments; effects of forced filtration, storage agitation, and high temperatures on hemostatic function

J Trauma Acute Care Surg
Volume 84, Number 6, Supplement 1

Joar Sivertsen, Hanne Braathen, Turid Helen F. Lunde, MSc, Philip C. Spinella, MD, Warren Dorlac, MD, Geir Strandenes, MD, Torunn O. Apelseth, PhD, Tor A. Hervig, PhD, *and* **Einar K. Kristoffersen, PhD**, *Bergen, Norway*

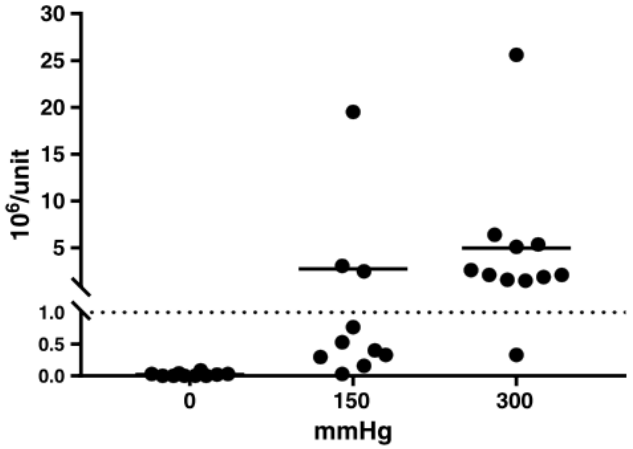


Figure 2. Residual WBC of individual whole blood units after LR with the Imuflex WB-SP filter (Terumo BCT). An irrigation pump was used to apply 0 mm Hg (n = 10, mean = 0.02), 150 mm Hg (n = 10, mean = 2.76, $p = 0.182$) or 300 mm Hg (n = 11, mean = 4.97, $p = 0.043$) pressure. *Solid lines* indicate means. *Dotted line* represents upper limit of 0.1×10^6 per unit recommended by guidelines. The mean values for 150 mm Hg and 300 mm Hg were compared to that of 0 mm Hg (gravity filtration) using the independent samples *t*-test with $\alpha = 0.05$.

TABLE 3. Storage at 4°C of Whole Blood Leukoreduced Using the Imuflex WB-SP Filter

	No Agitation				
	PF	**Day 0**	**Day 10**	**Day 14**	**Day 21**
General					
PLT, 10^9/L**	160 ± 19	158 ± 23	129 ± 22	127 ± 22	132 ± 30
HGB, g/dL	12.9 ± 1	12.8 ± 0.9	12.9 ± 0.9	13 ± 0.9	12.9 ± 0.9
RBC, 10^{12}/L	4 ± 0.3	3.9 ± 0.3	4 ± 0.3	4 ± 0.4	3.9 ± 0.3
TEG					
R, min	6.1 ± 1.1	7.6 ± 1.2	7.4 ± 0.6	7.3 ± 1	7.2 ± 0.7
K, min**	1.5 ± 0.2	1.8 ± 0.2	3 ± 0.3	3.3 ± 0.5	3.9 ± 0.9
Angle, degree**	67.3 ± 3.6	61.9 ± 3.2	51.6 ± 2.7	48.6 ± 4.6	47.6 ± 4.9
MA, mm**	61 ± 5.9	59.1 ± 4.3	54.2 ± 5	54 ± 4.5	50.5 ± 4.4
LY30, %*	0.3 ± 0.4	0.8 ± 0.9	0 ± 0	0 ± 0	0 ± 0
Multiplate					
ADP, U**	44 ± 9	27 ± 7	5 ± 2	3 ± 1	1 ± 1
AA, U**	30 ± 8	21 ± 7	4 ± 2	2 ± 1	1 ± 1
Ristocetin, U**	63 ± 12	47 ± 10	18 ± 7	12 ± 4	7 ± 4
TRAP-6, U**	78 ± 13	35 ± 6	8 ± 2	5 ± 2	2 ± 1

Effects of platelet-sparing leukocyte reduction and agitation methods on in vitro measures of hemostatic function in cold-stored whole blood

J Trauma Acute Care Surg
Volume 84, Number 6, Supplement 1

Kenneth E. Remy, MD, MHSc, Mark H. Yazer, MD, Arun Saini, MD, Ajlana Mehanovic-Varmaz, MPH, Sharon R. Rogers, MS, Andrew P. Cap, MD, PhD, *and* **Philip C. Spinella, MD, FCCM**, *St. Louis, Missouri*

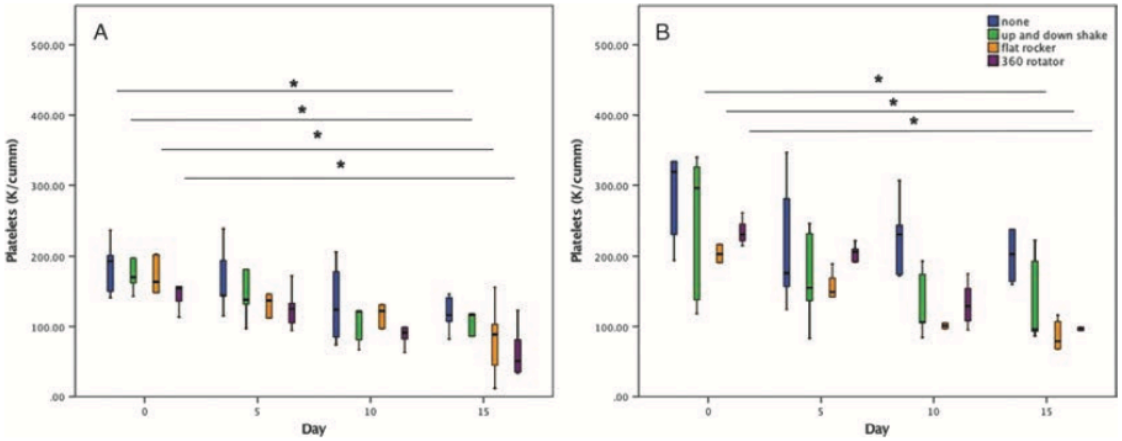
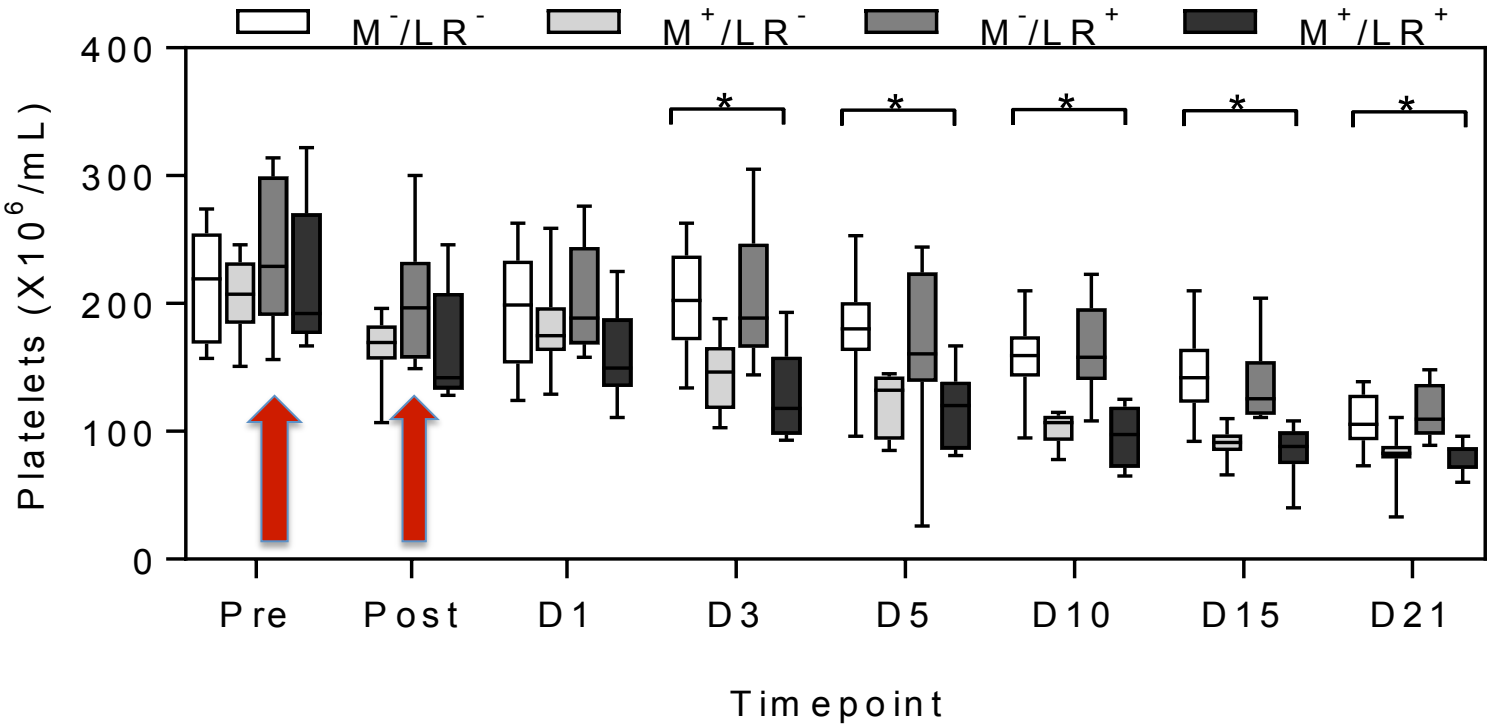


Figure 5. Platelet concentration in leukoreduced and nonleukoreduced and WB units by agitation method over time. This figure shows the platelet concentration of *LR* (*A*) and *non-LR* (*B*) WB units by differing agitation methods over 15 days. Whole blood was then randomized to four agitation methods; un-rocked (*blue bar*; *none*), *up and down shake* (*green bar*), continuous mechanical horizontal agitation via flat rocker (*yellow bar*), or continuous end-over-end rocking via a 360° rotator (*red*). Median platelet concentrations were compared at each time point for LR and non-LR units with no significant differences. Absolute median platelet concentrations were compared from Day 0 to Day 15 within each agitation method for LR and non-LR groups. The LR group had differences for all agitation methods, and the non-LR group had differences for up and down shake, flat rocker, and 360° rotator. Differences are indicated by $*p < 0.05$, $**p < 0.01$, $***p < 0.001$.

Unpublished Data

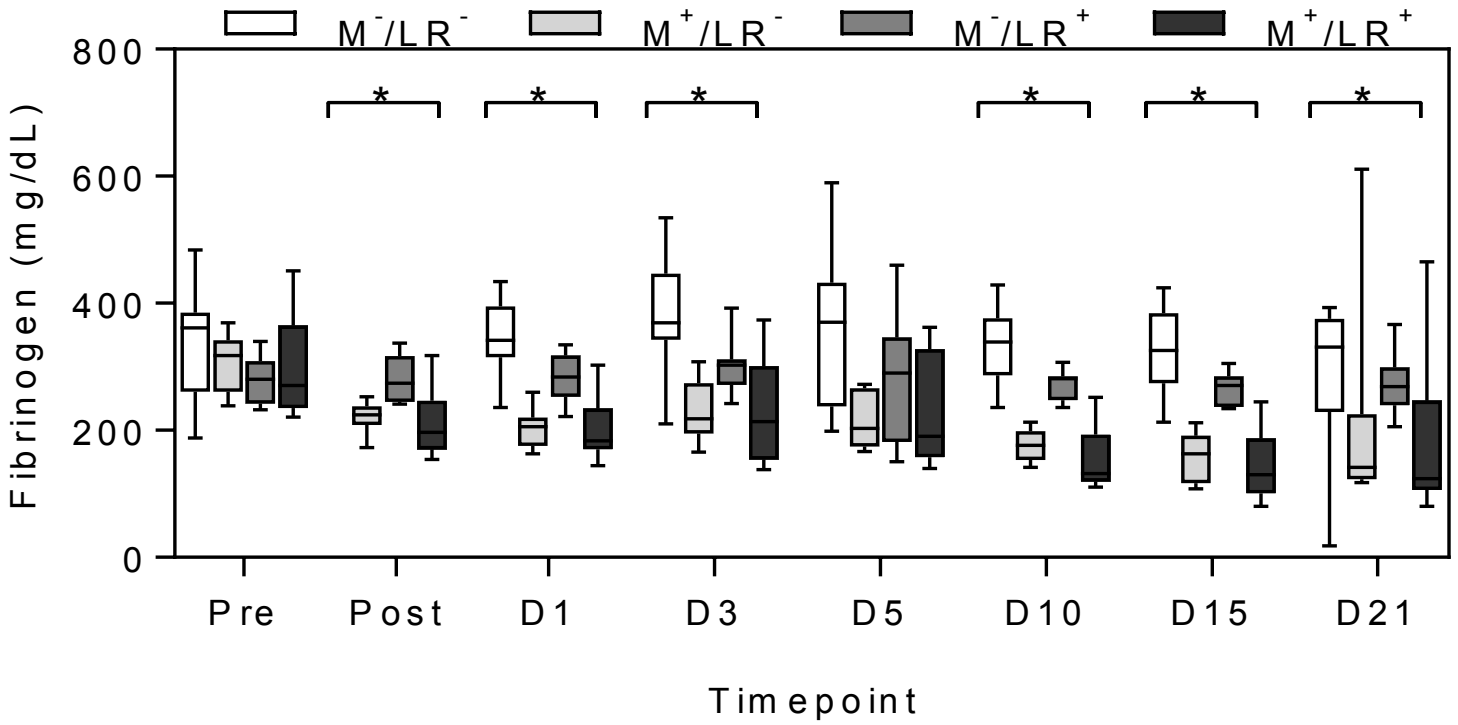
- Effect of Leukoreduction and Mirasol treatment on hemostatic measures in whole blood stored at 4C for 21 days
  - 8 samples in each study group

LR Does Not Reduce PLT Count



* Defines significant differences ($p<0.05$) between groups at a given time point.

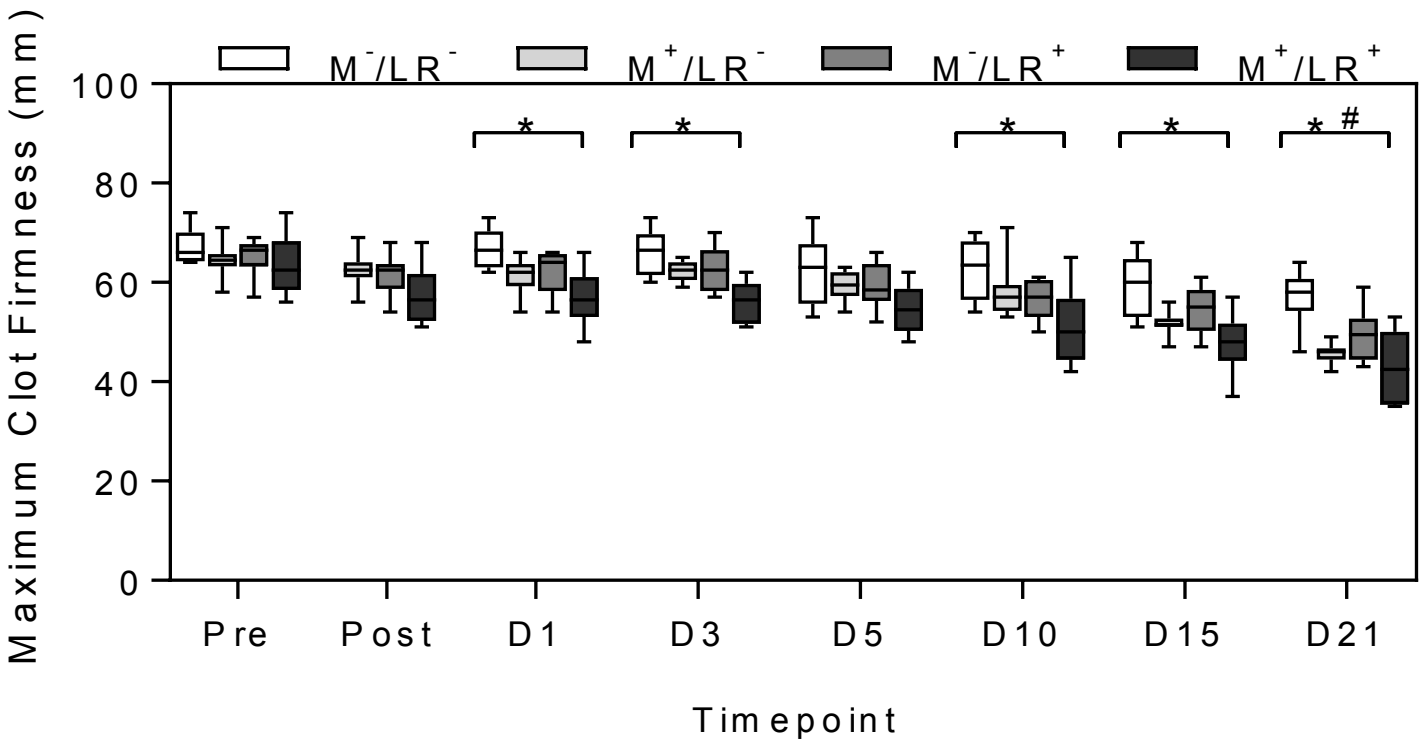
LR Does Not Reduce FGN



* Defines significant differences ($p<0.05$) between groups at a given time point.

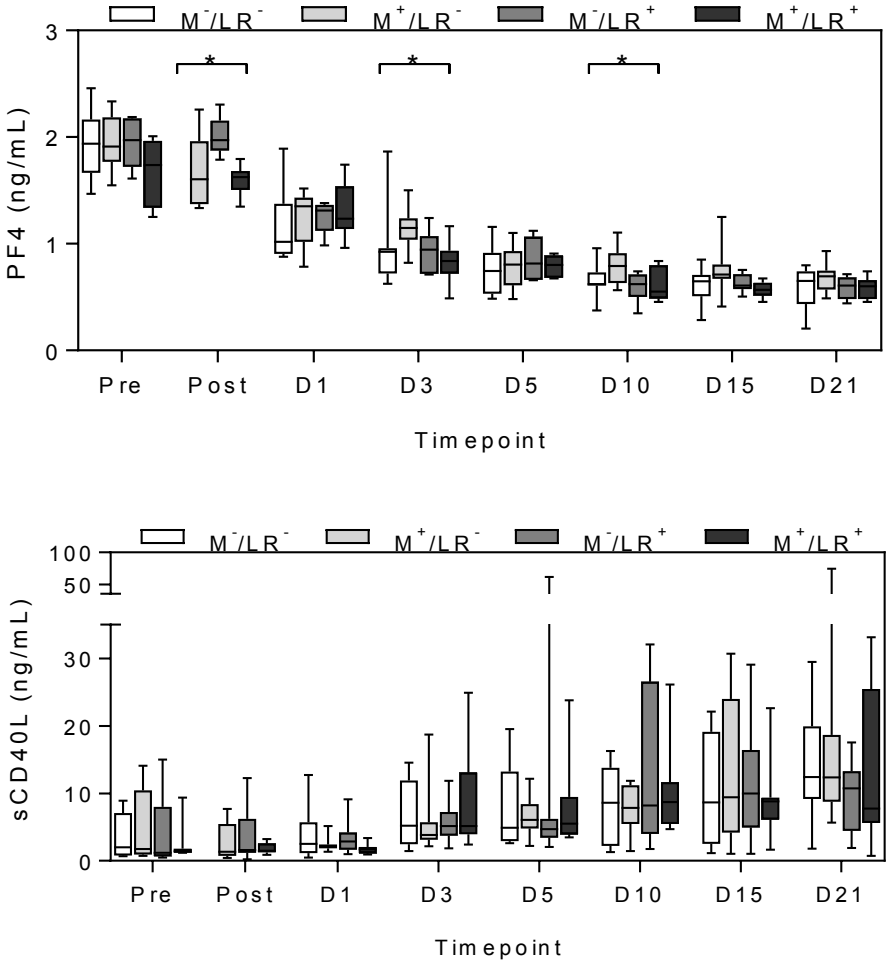
LR Does Not Reduce MCF

(except D21)



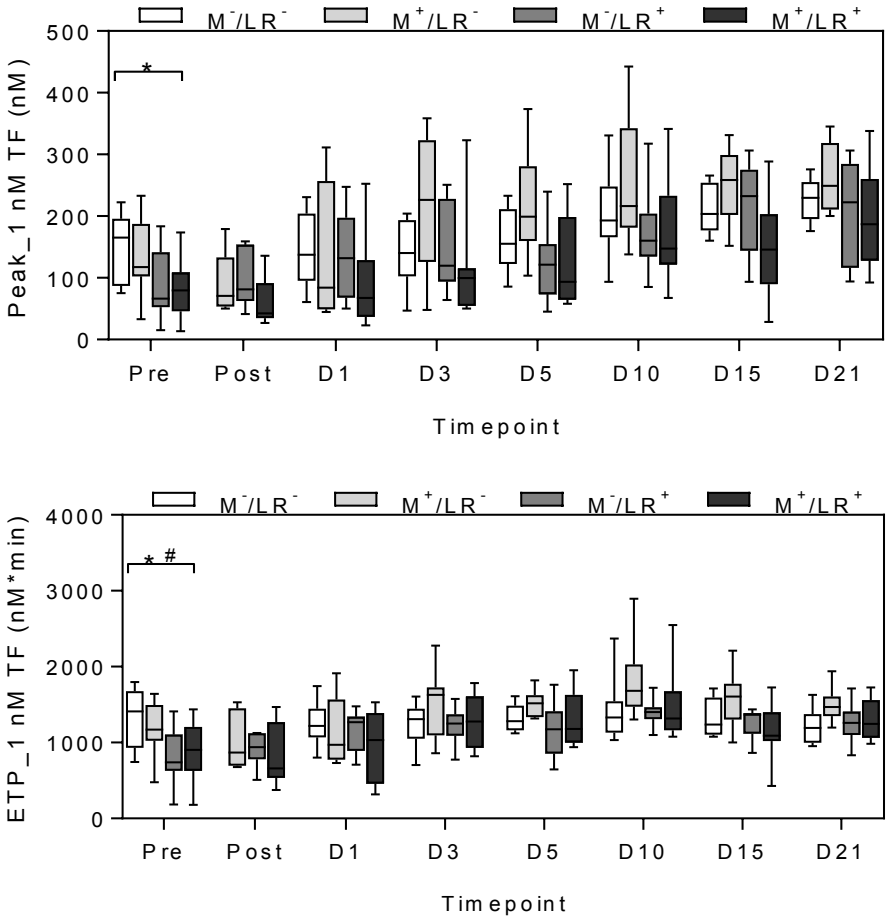
* Defines significant differences ($p<0.05$) between groups at a given time point.
# Defines a significance ($p<0.05$) directly between M-/LR- and M-/LR+ at a given time point.

LR Does Not Reduce PLT Activation Factors



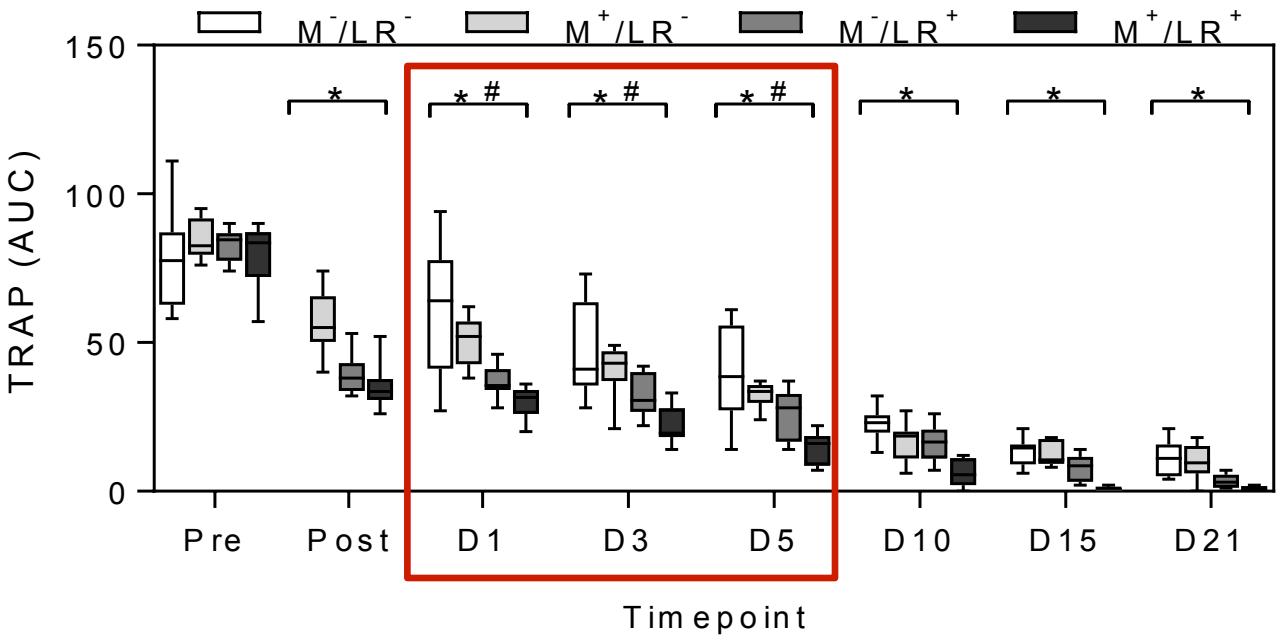
* Defines significant differences ($p<0.05$) between groups at a given time point.

LR Does Not Reduce Thrombin Generation



* Defines significant differences ($p<0.05$) between groups at a given time point.

LR Does Reduce Aggregation (D1-5)



* Defines significant differences ($p<0.05$) between groups at a given time point.
# Defines a significance ($p<0.05$) directly between M-/LR- and M-/LR+ at a given time point.

Data Summary

- LR with PLT sparing filter vs No LR
  - No differences for 21 days
    - PLT count
    - Fibrinogen concentration
    - TEG/ROTEM MA
    - Platelet activating factors
    - Thrombin generation
  - Difference day 1-5
    - Aggregation

Hemostatic Monitoring Limitations

- Impedance Aggregation
  - Response to single agonist
  - May underestimate in vivo platelet function
- Viscoelastic tests
  - TF or Kaolin activation
  - May overestimate in vivo platelet function
- Thrombin Generation
  - If platelet poor plasma used – NO PLATELETS

Conclusions

- Some benefits with leukoreduction
  - No clinical outcome benefits in trauma RCTs
- Leukoreduction might reduce aggregation
  - Only day 1-5
- Leukoreduction increase cost

Conclusions

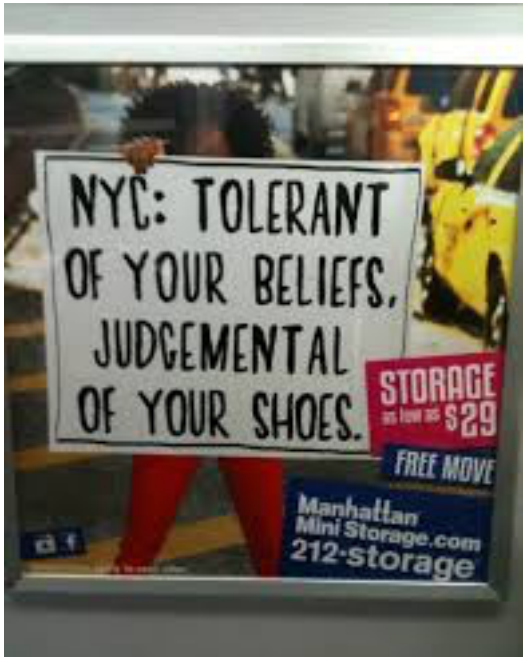
- If you must LR you probably don't lose much hemostatic effect
- If you don't LR you probably are not sacrificing outcomes

Questions?


Poles Are For Your Safety, Not Your Latest Routine
Hold the pole, not our attention. A subway car is no place for showtime.
12


Please do not smile at strangers
14 St
failblog.org


Meanwhile In New York...
ALWAYS OFFER YOUR SEAT TO A PREGNANT WOMAN.
UNLESS SHE'S WEARING A RED SOX HAT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