Published in final edited form as:

J Trauma Acute Care Surg. 2016 April ; 80(4): 568–575. doi:10.1097/TA.0000000000000960.

Damage Control Resuscitation And Emergency Laparotomy: Findings From The PROPPR Study

Vicente J. Undurraga Perl, MD [Resident],

Department of Surgery, Oregon Health & Science University, undurrag@ohsu.edu

Brian Leroux, PhD [Professor],

Department of Biostatistics, University of Washington, leroux@uw.edu

Mackenzie R. Cook, MD [Chief Resident],

Department of Surgery, Oregon Health & Science University, cookmac@ohsu.edu

Justin Watson, MD [Resident],

Department of Surgery, Oregon Health & Science University, watsonju@ohsu.edu

Kelly Fair, MD [Chief Resident],

Department of Surgery, Oregon Health & Science University, fair@ohsu.edu

David T. Martin, MD [Resident],

Department of Surgery, University of California San Francisco-East Bay, martida@ohsu.edu

Jeffrey D. Kerby, MD, PhD [Professor],

Division of Trauma, Burns, and Surgical Critical Care, University of Alabama, jkerby@uabmc.edu

Carolyn Williams, RN, BSN, BSME [Research Nurse],

Name and Address for correspondence: Vicente J. Undurraga Perl MD, Department of Surgery, Oregon Health & Science University, 3181 S.W. Sam Jackson Park Road, Portland, OR 97239-3098, United States of America, phone 503-494-8211; fax: 503-494-5615, undurrag@ohsu.edu.

Conflicts of Interest and Source of Funding:

For all authors, no conflicts were declared

List of meetings at which the paper was presented

This study was presented at the 74th annual meeting of the American Association for the Surgery of Trauma, September 9–12, 2015, in Las Vegas, Nevada.

Author Contribution:

Vicente J. Undurraga Perl MD: literature search, study design, data interpretation, writing

Brian Leroux PhD: Data analysis and interpretation, writing

Mackenzie R. Cook MD: study design, critical revision

Justin Watson MD: data collection

Kelly Fair MD: writing, critical revision

David T. Martin MD: literature search, study design, critical revision

Jeffrey D. Kerby MD, PhD: study design, critical revision

Carolyn Williams RN, BSN: study implementation

Kenji Inaba MD: critical revision

Charles E. Wade PhD: critical revision, writing, data interpretation

Bryan A. Cotton MD, MPH: critical revision

Deborah J Del Junco, PhD: data interpretation, critical revision

Erin E. Fox PhD: study design, data interpretation, critical revision

Thomas M. Scalea MD: study design, critical revision

Barbara C. Tilley PhD: study design, data interpretation

John B. Holcomb MD: study design, data interpretation

Martin A. Schreiber MD: study design, data interpretation, writing and critical revision

University of Alabama, cswilliams@uabmc.edu

Kenji Inaba, MD [Associate Professor],

Division of Trauma & Critical Care University of Southern California, Kenji.Inaba@med.usc.edu

Charles E. Wade, PhD [Professor],

Center for Translational Injury Research, Division of Acute Care Surgery, Department of Surgery, Medical School, University of Texas Health Science Center at Houston, Charles.E.Wade@uth.tmc.edu

Bryan A. Cotton, MD, MPH [Professor],

Center for Translational Injury Research, Division of Acute Care Surgery, Department of Surgery, Medical School, University of Texas Health Science Center at Houston, bryan.a.cotton@uth.tmc.edu

Deborah J Del Junco, PhD [Associate Professor],

Center for Translational Injury Research, Division of Acute Care Surgery, Department of Surgery, Medical School, University of Texas Health Science Center at Houston, Deborah.J.DelJunco@uth.tmc.edu

Erin E. Fox, PhD [Assistant Professor],

Center for Translational Injury Research, Division of Acute Care Surgery, Department of Surgery, Medical School, University of Texas Health Science Center at Houston, erin.e.fox@uth.tmc.edu

Thomas M. Scalea, MD [Physician in Chief],

Shock Trauma Center, University of Maryland School of Medicine, tscalea@umm.edu

Barbara C. Tilley, PhD [Professor],

Division of Biostatistics, School of Public Health, University of Texas Health Science Center at Houston, Barbara.C.Tilley@uth.tmc.edu

John B. Holcomb, MD [Professor], and

Center for Translational Injury Research, Division of Acute Care Surgery, Department of Surgery, Medical School, University of Texas Health Science Center at Houston, John.Holcomb@uth.tmc.edu

Martin A. Schreiber, MD [Professor]

Division of Trauma, Critical Care & Acute Surgery, Oregon Health & Science University, schreibm@ohsu.edu

on behalf of the PROPPR Study Group

Abstract

Background—The Pragmatic Randomized Optimal Platelet and Plasma Ratios (PROPPR) trial has demonstrated that damage control resuscitation, a massive transfusion strategy targeting a balanced delivery of plasma-platelet-RBC in a ratio of 1:1:1, results in improved survival at 3 hours and a reduction in deaths due to exsanguination in the first 24 hours compared to a 1:1:2 ratio. In light of these findings, we hypothesized that patients receiving 1:1:1 ratio would have improved survival after emergency laparotomy.

Methods—Severely injured patients predicted to receive a massive transfusion admitted to 12 level I North American trauma centers were randomized to 1:1:1 versus 1:1:2 as described in the PROPPR trial. From these patients, the subset that underwent an emergency laparotomy, defined previously in the literature as laparotomy within 90 minutes of arrival, were identified. We compared rates and timing of emergency laparotomy as well as post-surgical survival at 24-hours and 30-days.

Results—Of the 680 enrolled patients, 613 underwent a surgical procedure, 397 underwent a laparotomy, and 346 underwent an emergency laparotomy. The percentages of patients undergoing emergency laparotomy were 51.5% (174/338) and 50.3% (172/342) for 1:1:1 and 1:1:2, respectively ($p=0.20$). Median time to laparotomy was 28 minutes in both treatment groups. Among patients undergoing an emergency laparotomy, the proportions of patients surviving to 24 hours and 30 days were similar between treatment arms, 24-hour survival was 86.8% (151/174) for 1:1:1 and 83.1% (143/172) for 1:1:2 ($p=0.29$), and 30-day 79.3% (138/174) for 1:1:1 and 75.0% (129/172) for 1:1:2 ($p=0.30$).

Conclusions—We found no evidence that resuscitation strategy affects whether a patient requires an emergency laparotomy, time to laparotomy, or subsequent survival.

Level of Evidence—Level IV, therapeutic study.

Keywords

damage control resuscitation; emergency laparotomy; PROPPR

Background

Resuscitation of trauma patients is in constant evolution.¹ Until recently, early resuscitation of trauma patients has focused on aggressive resuscitation with crystalloid and packed red blood cells (RBCs) resulting in recurrent bleeding, exacerbation of the acute coagulopathy of trauma, excessive edema and increased incidence of multiple organ failure. The damage control resuscitation paradigm developed by the US military focuses on early hemorrhage control, minimization of crystalloid and the delivery of plasma, platelets and RBCs in a 1:1:1 ratio. This approach is being widely adopted by civilian trauma centers.

There is a large volume of retrospective data that suggest that high ratio transfusion results in improved survival in patients who require massive transfusion.^{2, 3} However, a significant survival difference at 24 hours or 30 days was not demonstrated in association with a 1:1:1 transfusion ratio compared to a 1:1:2 ratio in the Pragmatic Randomized Optimal Platelet and Plasma Ratios (PROPPR) trial.⁴ High ratio transfusion was associated with improved survival at 3 hours and a reduction in deaths due to exsanguination at 24 hours.⁴

Severely injured trauma patients undergoing resuscitation frequently require multiple procedures.⁵ The most frequent procedure required early after patient presentation is an emergency laparotomy.⁶ Timing of emergency laparotomy was studied in a 2002 paper by Clarke et al.⁷ that showed that, among hypotensive, severely injured trauma patients undergoing laparotomy within 90 minutes, mortality increased by 1% for each 3 additional

minutes spent in the ED. While performed commonly, over the last decade, there are few studies of resuscitation or timing of trauma laparotomy.

In addition to time to OR, fluid management is a critical aspect of the management of trauma patients who require emergency laparotomy. Uncontrolled truncal hemorrhage is exacerbated by aggressive fluid resuscitation with crystalloid, and a high ratio transfusion strategy would theoretically avoid exacerbation of the acute coagulopathy of trauma and associated adverse outcomes. Among patients undergoing a damage control laparotomy, a high ratio transfusion strategy has been associated with decreased resuscitation volumes and mortality.⁸

Given the previously published literature showing associations between damage control resuscitation and decreased mortality², decreased time to OR⁷ and reduced mortality, and the early survival advantage demonstrated in the PROPPR trial, we hypothesized that patients receiving a 1:1:1 transfusion of plasma:platelets:RBCs would have improved survival after emergency laparotomy compared to patients receiving a 1:1:2 ratio.

Methods

The PROPPR trial was performed under Exception From Informed Consent (EFIC) guidelines and approved by all institutional review boards at participating hospitals. Severely injured patients predicted to receive a massive transfusion and admitted to 12 level I North American trauma centers were randomized to a 1:1:1 ratio of plasma:platelets:RBCs versus a 1:1:2 ratio as described in the PROPPR trial.⁴ Of the 680 patients randomized in PROPPR, the subset that underwent an emergency laparotomy (E-LAP) within 90 minutes of hospital arrival was identified. The 90 minute cutoff was chosen given the relationship between increasing time in the ED up to 90 minutes and mortality in hypotensive patients undergoing laparotomy for trauma.⁷ In addition, this cutoff was chosen to reduce survival bias compared to a longer time period, given that patients who die early may not live long enough to have a laparotomy. The two randomized treatment groups were compared with respect to rates of surgical procedures performed (in addition to laparotomy), survival to 3, 6, 12, 24, and 72 hours, survival to 30 days, death due to exsanguination or hemorrhagic shock, units of blood products received during the randomized treatment period and in the first 24 hours from arrival, hospital-free days, ICU-free days, ventilator-free days, rates of acute kidney injury, multi-system organ failure, and acute respiratory distress syndrome; and disposition at 30 days (discharged to home, remained hospitalized, discharged to morgue, or other). Differences between treatment groups were assessed for statistical significance and 95% confidence intervals were calculated using robust variance estimates of Generalized Estimating Equations to accommodate non-constant variance. All group comparisons were adjusted for site using indicator variables. Additional analyses were conducted with adjustment for additional baseline covariates, including age, gender, race, Hispanic ethnicity, base deficit, vital signs, and injury severity scores; covariates with more than 10% missing data (diastolic blood pressure, Fast Exam, INR, TEG r-time, and ATC) were not controlled in these analyses.

Kaplan-Meier survival curves and 95% confidence intervals were graphed for each treatment group over the first 24 hours starting from the time of initial visit to the OR. Cox proportional hazards regression models were fit to compare death rates in the two treatment groups with adjustment for site. Differences between sites in rates of emergency laparotomy were assessed using random effects models. Statistical analyses were performed using R (Version 3.2.0, <http://www.R-project.org/>).

Results

Of the 680 patients enrolled in PROPPR, 613 underwent a surgical procedure with 397 receiving a laparotomy, of which 346 were E-LAPs (within 90 minutes of arrival). Laparotomies occurred between 90 and 120 minutes for 19 patients and more than 120 minutes for 32 patients. The percentages of patients undergoing an E-LAP were 51.5% (174/338) and 50.3% (172/342) for 1:1:1 and 1:1:2, respectively. Baseline demographics, injury severity, baseline hemodynamics and labs for patients with and without an E-LAP stratified by treatment groups are demonstrated in table 1. Median time to laparotomy from admission was 28 minutes in both treatment groups. Of the 346 patients with an E-LAP, 194 (56%) went to the OR for the laparotomy prior to randomization whereas 152 (44%) went to the OR after randomization.

There were differences between the treatment groups in the types of procedures performed during the first OR visit (table 2). The 1:1:1 group had a greater number of small intestine procedures, large intestine procedures as well as fracture reduction and/or fixation. The most common procedures in both groups were related to damage control laparotomy and included abdominal packing (35.8%) and temporary abdominal closure (38.7%). While there was a trend toward higher numbers of solid organ procedures and lower rates of abdominal packing in the 1:1:2 group, these differences were not statistically significant.

Adjusting for site, the volume of RBCs and platelets transfused during randomization and over the first 24 hours differed among treatment groups (table 3). Patients in the 1:1:1 group received more plasma during the randomized treatment period but that difference did not persist to 24 hours. Patients in the 1:1:1 group received more platelets during the randomized treatment period and at 24 hours. Hospital-free days, ICU-free days and ventilator-free days were similar between groups. Patients also had similar rates of acute kidney injury, multiple organ failure, acute respiratory distress syndrome, and disposition at 30 days (table 3).

Among patients undergoing an E-LAP within 90 minutes, Kaplan-Meier survival curves were not significantly different by resuscitation group (see Figure 1). Kaplan-Meier curves were also examined for periods from 3 hours to 30 days and no significant differences were found (figures not shown). 24-hour survival was 86.8% (151/174) for 1:1:1 and 83.1% (143/172) for 1:1:2 ($p=0.29$), and 30-day survival was 79.3% (138/174) for 1:1:1 and 75.0% (129/172) for 1:1:2 ($p=0.30$).

There were no differences between treatment groups in mortality rates by Cox proportional hazards regression: hazard ratio 0.78, 95% confidence interval 0.50 to 1.21, $p = 0.27$ (Table

4). There were also no differences in survival rates by site ($p=0.74$). Although the observed proportions of patients with an E-LAP ranged from 29% to 64% among the different centers participating in the PROPPR trial, these differences were not statistically significant possibly due to small sample sizes in some centers. The overall E-LAP rate for patients enrolled in PROPPR was 51% and survival of these patients was 77% at 30 days.

In a sensitivity analysis, models were refit including only the subset of 194 patients who went to the OR for the E-LAP prior to randomization. The results in these analyses were qualitatively similar to the results from the entire sample of 346 patients; in particular, no differences in survival between treatment groups were found.

Discussion

Exsanguination has been shown to be a leading cause of death in severely injured trauma patients. In a series by Cripps et al,⁹ 33% of patients who died while being massively transfused (either a massive transfusion or massive transfusion activation) died from exsanguination, which was the second leading cause of death from trauma in this series. The overall death rate reported in the Cripps study was 40%, which is higher than the 22.8% overall 30-day mortality rate reported in this subset of patients enrolled in PROPPR. The improvement in overall mortality rate may be attributed to recent improvements in resuscitation.

In a secondary analysis of the PRospective Observational Multicenter Major Trauma Transfusion (PROMMTT) study, patients who had a laparotomy within 90 minutes of admission and had a FAST exam were analyzed. This analysis showed increased 24 hour mortality with increasing time to operation, with a hazard ratio of 1.5 for each 10 minutes.⁶ While this paper described the different procedures performed and had similarly high injury severity and low mortality rate, it focused primarily on blunt trauma patients (64.5%) compared with our sample which included only 44.2% of patients with blunt injuries. In addition, patients enrolled in PROMMTT were not randomized to different transfusion ratios and deaths within 30 minutes of admission were excluded. Ultimately, overall mortality rates were similar in the two studies.

Although we found higher rates of small and large intestine procedures as well as fracture reduction and/or fixation in the 1:1:1 group compared to the 1:1:2 group, these results should be interpreted with caution because of the possibility that they represent type I errors, given that a large number of statistical tests were performed. Further research is needed to attempt to verify these findings and to explore possible mechanisms. In addition, this study failed to show a difference in rates of emergency laparotomy or 30 day survival among participating centers. The low overall mortality rate of 22.8% compared to prior studies may have made it difficult to observe a treatment effect. Thirdly, because the data set analyzed here included only 346 patients with emergency laparotomies, the power may not have been sufficient to detect a difference between treatments. Another limitation of this study is the potential for bias due to the use of post-randomization information (some patients went to the operating room for an emergency laparotomy after randomization); although similar results were found in a sensitivity analysis using only those patients going to the operating

room prior to randomization, the potential for bias remains. Together, these limitations may present opportunities for further research to confirm our findings.

In this study, we did not find a significant difference in survival from 3 hours to 30 days, complications or discharge disposition among severely injured trauma patients enrolled in PROPPR who underwent an E-LAP and were randomized to a 1:1:1 vs a 1:1:2 ratio of plasma:platelets:RBCs. We did, however, find significant differences in volumes of plasma and platelets transfused during the randomized treatment period, which confirms the quality of the main PROPPR study's design and execution. As shown in the PROPPR analysis⁴, this difference became less significant with increasing time since hospital arrival, with the 1:1:2 patients approaching the same volume of transfusion of plasma and platelets as the 1:1:1 group, potentially decreasing any treatment benefit of a high ratio transfusion. Even though the patient's in the 1:1:2 group received fewer platelets at randomization and 24 hours, and had delayed access to platelets, only receiving platelet transfusions with the second box of blood, after 3 units of plasma and 6 units of pRBCs, we found both transfusion strategies to result in similar outcomes.

While this is a post-hoc analysis of patients previously randomized in PROPPR, the groups appeared similar in baseline characteristics. Given the sample of patients was accrued across multiple level I trauma centers in North America, between August 2012 and December 2013, our findings may be applicable to other level I trauma centers in North America in the near future. In contrast, these results may not be as applicable in rural America and the developing world, where RBCs, thawed plasma and platelets are in limited supply, limiting access to therapies, such as damage control resuscitation. To improve trauma care in these settings, novel blood products^{10, 11}, such as lyophilized plasma¹², and freeze dried platelets are being developed but are not yet available in the United States.

Conclusion

Among severely injured trauma patients who met enrollment criteria for PROPPR and who underwent an E-LAP, we were unable to detect significant differences between a 1:1:1 ratio of plasma:platelets:RBCs versus a 1:1:2 ratio as measured by the frequency of E-LAPs, time to E-LAPs, disposition at 30 days or survival.

Acknowledgments

We would like to acknowledge Christopher Connelly MD and John Yonge MD for their help with data collection and Katherine Block VMD for her help with the manuscript.

Disclosures of funding received for this work

The Pragmatic, Randomized Optimal Platelet and Plasma Ratios (PROPPR) trial was sponsored by the U.S. National Heart, Lung, and Blood Institute (U01HL077863), the U.S. Department of Defense, as well as Defense Research and Development Canada in partnership with the Canadian Institutes of Health Research (CIHR), Institute of Circulatory and Respiratory Health (CRR-120612). The opinions or conclusions contained herein are the private views of the authors and are not to be construed as official or as reflecting the views of any sponsor. This manuscript has been reviewed by the PROPPR Publication Committee for scientific content and consistency of data interpretation with previous PROPPR publications.

REFERENCES

1. Martin DT, Schreiber MA. Modern resuscitation of hemorrhagic shock: What is on the horizon? *Eur J Trauma Emerg S.* 2014; 40:641–656.
2. Holcomb JB, del Junco DJ, Fox EE, Wade CE, Cohen MJ, Schreiber MA, Alarcon LH, Bai Y, Brasel KJ, Bulger EM, et al. The prospective, observational, multicenter, major trauma transfusion (PROMTTT) study: Comparative effectiveness of a time-varying treatment with competing risks. *JAMA Surg.* 2013; 148:127–136. [PubMed: 23560283]
3. Duchesne JC, Heaney J, Guidry C, McSwain N Jr, Meade P, Cohen M, Schreiber M, Inaba K, Skiada D, Demetriades D, et al. Diluting the benefits of hemostatic resuscitation: A multi-institutional analysis. *J Trauma Acute Care Surg.* 2013; 75:76–82. [PubMed: 23778442]
4. Holcomb JB, Tilley BC, Baraniuk S, Fox EE, Wade CE, Podbielski JM, del Junco DJ, Brasel KJ, Bulger EM, Callcut RA, et al. Transfusion of plasma, platelets, and red blood cells in a 1:1:1 vs a 1:1:2 ratio and mortality in patients with severe trauma: The PROPPR randomized clinical trial. *JAMA.* 2015; 313:471–482. [PubMed: 25647203]
5. Semmlow JL, Cone R. Utility of the injury severity score: A confirmation. *Health Serv Res.* 1976; 11:45–52. [PubMed: 965234]
6. Barbosa RR, Rowell SE, Fox EE, Holcomb JB, Bulger EM, Phelan HA, Alarcon LH, Myers JG, Brasel KJ, Muskat P, et al. Increasing time to operation is associated with decreased survival in patients with a positive FAST examination requiring emergent laparotomy. *J Trauma Acute Care Surg.* 2013; 75:S48–S52. [PubMed: 23778511]
7. Clarke JR, Trooskin SZ, Doshi PJ, Greenwald L, Mode CJ. Time to laparotomy for intra-abdominal bleeding from trauma does affect survival for delays up to 90 minutes. *J Trauma.* 2002; 52:420–425. [PubMed: 11901314]
8. Cotton BA, Reddy N, Hatch QM, LeFebvre E, Wade CE, Kozar RA, Gill BS, Albarado R, McNutt MK, Holcomb JB. Damage control resuscitation is associated with a reduction in resuscitation volumes and improvement in survival in 390 damage control laparotomy patients. *Ann Surg.* 2011; 254:598–605. [PubMed: 21918426]
9. Cripps MW, Kutcher ME, Daley A, McCreery RC, Greenberg MD, Cachola LM, Redick BJ, Nelson MF, Cohen MJ. Cause and timing of death in massively transfused trauma patients. *J Trauma Acute Care Surg.* 2013; 75:S255–S262. [PubMed: 23883917]
10. Cap AP, Pidcock HF, DePasquale M, Rappold JF, Glassberg E, Eliassen HS, Bjerkvig CK, Fosse TK, Kane S, Thompson P, et al. Blood far forward: Time to get moving! *J Trauma Acute Care Surg.* 2015; 78:S2–S6. [PubMed: 26002259]
11. Jenkins D, Stubbs J, Williams S, Berns K, Zielinski M, Strandenes G, Zietlow S. Implementation and execution of civilian remote damage control resuscitation programs. *Shock.* 2014; 41(Suppl 1):84–89. [PubMed: 24662783]
12. McCully SP, Martin DT, Cook MR, Gordon NT, McCully BH, Lee TH, Dean RK, Rick EA, Moren AM, Fair KA, et al. Effect of ascorbic acid concentrations on hemodynamics and inflammation following lyophilized plasma transfusion. *J Trauma Acute Care Surg.* 2015; 79:30–38. [PubMed: 26091311]

Pragmatic, Randomized Optimal Platelet and Plasma Ratios (PROPPR) Study Group

Clinical Coordinating Center: John B. Holcomb, MD; Charles E. Wade, PhD; Deborah J. del Junco, PhD; Erin E. Fox, PhD; Nena Matijevic, PhD (Laboratory Committee co-Chair); Jeanette Podbielski, RN; Angela M. Beeler, BS.

Data Coordinating Center: Barbara C. Tilley, PhD; Sarah Baraniuk, PhD; Joshua Nixon, MS; Roann Seay, MS; Savitri N. Appana, MS; Hui Yang, MS; Michael O. Gonzalez, MS.

Core Laboratory: Lisa Baer, MS; Yao-Wei Willa Wang, MD; Brittany S. Hula, MS; Elena Espino, BS; An Nguyen, BS; Nicholas Pawelczyk, BS; Kisha D. Arora-Nutall, BS; Rishika Sharma, MD; Jessica C. Cardenas, PhD; Elaheh Rahbar, PhD; Tyrone Burnett, Jr., BS; David Clark, BS.

Resuscitation Outcomes Consortium: Gerald van Belle, PhD; Susanne May, PhD; Brian Leroux, PhD; David Hoyt, MD; Judy Powell, BSN, RN; Kellie Sheehan, BSN.

Systems Biology Committee: Alan Hubbard, PhD (co-Chair); Adam P. Arkin, PhD.

Transfusion Committee: John R. Hess, MD (co-Chair); Jeanne Callum, MD (co-Chair)

PROPPR Clinical Sites (listed in order of number of patients enrolled):

University of Texas Health Science Center at Houston: Bryan A. Cotton, MD, MPH; Laura Vincent, BSN, RN, CCRP; Timothy Welch; Tiffany Poole, DC; Evan G. Pivalizza, MD; Sam D. Gumbert, MD; Yu Bai, MD, PhD; James J. McCarthy, MD; Amy Noland, MD; Rhonda Hobbs, MT(ASCP)SBB.

University of Washington: Eileen M. Bulger, MD; Patricia Klotz, RN; Lindsay Cattin, BA; Keir J. Warner, BS; Angela Wilson, BA; David Boman, BA; Nathan White, MD, MS; Andreas Grabinsky, MD; Jennifer A. Daniel-Johnson, MBBS.

University of California, San Francisco: Mitchell Jay Cohen, MD (Systems Biology and Laboratory Committees co-Chair); Rachael A. Callcut, MD, MSPH; Mary Nelson, RN, MPA; Brittney Redick, BA; Amanda Conroy, BA; Marc P. Steurer, MD, DESA; Preston C. Maxim, MD; Eberhard Fiebig, MD; Joanne Moore; Eireen Mallari, MT.

University of Cincinnati: Peter Muskat, MD; Jay A. Johannigman, MD; Bryce R. H. Robinson, MD; Richard D. Branson, MSc, RRT; Dina Gomaa, BS, RRT; Christopher Barczak, BS, MT(ASCP); Suzanne Bennett, MD; Patricia M. Carey, MD; Christopher N. Miller, MD; Helen Hancock, BS, MT(ASCP); Carolina Rodriguez, BA.

University of Southern California: Kenji Inaba, MD; Jay G. Zhu, MD; Monica D. Wong, MS; Michael Menchine, MD, MPH; Kelly Katzberg, MD, FACEP; Sean O. Henderson, MD; Rodney McKeever, MD; Ira A. Shulman, MD; Janice M. Nelson, MD; Christopher W. Tuma, BA, MT(ASCP), SBB; Cheryl Y. Matsushita, BS, MT(ASCP).

Shock, Trauma and Anesthesiology Research - Organized Research Center (STAR-ORC), R Adams Cowley Shock Trauma Center, University of Maryland Medical Center: Thomas M. Scalea, MD; Deborah M. Stein, MD, MPH; Cynthia K. Shaffer, MS, MBA; Christine Wade, BA; Anthony V. Herrera, MS; Seeta Kallam, MBBS; Sarah E. Wade, BS; Samuel M. Galvagno, Jr, DO, PhD; Magali J. Fontaine, MD, PhD; Janice M. Hunt, BS, MT(ASCP) SBB; Rhonda K. Cooke, MD.

University of Tennessee Health Science Center, Memphis: Timothy C. Fabian, MD; Jordan A. Weinberg, MD; Martin A. Croce, MD; Suzanne Wilson, RN; Stephanie Panzer-Baggett, RN; Lynda Waddle-Smith, BSN; Sherri Flax, MD.

Medical College of Wisconsin: Karen J. Brasel, MD, MPH; Pamela Walsh, AS, CCRC; David Milia, MD; Allia Nelson, BS, BA; Olga Kaslow, MD, PhD; Tom P. Aufderheide, MD, MS; Jerome L. Gottschall, MD; Erica Carpenter, MLS(ASCP).

University of Arizona: Terence O’Keeffe, MBChB, MSPH; Laurel L. Rokowski, RN, BSN, MKT; Kurt R. Denninghoff, MD; Daniel T. Redford, MD; Deborah J. Novak, MD; Susan Knoll, MS, MT(ASCP) SBB.

University of Alabama at Birmingham: Jeffrey D. Kerby, MD, PhD; Jean-Francois Pittet, MD (Anesthesia Chair); Patrick L. Bosarge, MD; Albert T. Pierce, MD; Carolyn R. Williams, RN, BSN, BSME; Shannon W. Stephens, EMTP; Henry E. Wang, MD, MS ; Marisa B. Marques, MD.

Oregon Health and Science University: Martin A. Schreiber, MD ; Jennifer M. Watters, MD; Samantha J. Underwood, MS; Tahnee Groat, MPH; Craig Newgard, MD, MPH; Matthias Merkel, MD, PhD ; Richard M. Scanlan, MD; Beth Miller, MT(ASCP)SBB.

Sunnybrook Health Science Center: Sandro Rizoli, MD, PhD; Homer Tien, MD; Barto Nascimento, MD, MSc, CTBS; Sandy Trpcic; Skeeta Sobrian-Couroux, RN, CCRP, BHA; Marciano Reis; Adic Pérez, MD; Susan E. Belo, MD, PhD; Lisa Merkley, BA, MLT, CBTS; Connie Colavecchia, BSc, MLT.

Figure 1. Kaplan-Meier Survival Curves with 95% Confidence Intervals by Treatment Group During the Initial 6 Hours From the First Visit to the OR for Patients with an Emergency Laparotomy within 90 Minutes of Arrival (E-LAP)
Baseline (time 0) was set as the time of first visit to the operating room. The bold lines are Kaplan-Meier survival curve estimates and the thin lines are 95% confidence intervals.

Table 1
Baseline Characteristics Among Patients Who Underwent An Emergency Laparotomy
within 90 Minutes of Arrival (E-LAP), Stratified By Treatment Group

Baseline characteristics are described for patients who did not undergo E-LAP and for patients who underwent an E-LAP overall and stratified by the 1:1:1 and 1:1:2 treatment groups.

Characteristic	Patients Without Emergency Laparotomy (N = 334)	Patients with Emergency Laparotomy		
		Overall (N = 346)	1:1:1 Group (N = 174)	1:1:2 Group (N = 172)
Age, y, median (IQR)	37 (25, 54)	32 (24, 46)	32.5 (24, 49)	31.5 (24, 44)
Male sex, n (%)	264 (79.0%)	282 (81.5%)	137 (78.7%)	145 (84.3%)
Race, n (%)				
White	242 (72.5%)	192 (55.5%)	91 (52.3%)	101 (58.7%)
Black	58 (17.4%)	129 (37.3%)	67 (38.5%)	62 (36.0%)
Other	34 (10.2%)	25 (7.2%)	16 (9.2%)	9 (5.2%)
Hispanic Ethnicity, n (%)	61 (18.3%)	59 (17.1%)	25 (14.4%)	34 (19.8%)
GCS, median (IQR)	12 (3, 15)	14 (3, 15)	14 (6, 15)	14 (3, 15)
ISS, median (IQR)	26 (16, 38)	27 (18, 41)	28 (18.2, 41)	26 (18, 41)
Head AIS 3, n (%)	91 (27.2%)	62 (17.9%)	27 (15.5%)	35 (20.3%)
Chest AIS 3, n (%)	198 (59.3%)	215 (62.1%)	102 (58.6%)	113 (65.7%)
Abdomen AIS 3, n (%)	77 (23.1%)	263 (76.0%)	138 (79.3%)	125 (72.7%)
Extremity AIS 3, n (%)	174 (52.1%)	125 (36.1%)	63 (36.2%)	62 (36.0%)
Mechanism of Injury, (%blunt)	205 (61.4%)	153 (44.2%)	74 (42.5%)	79 (45.9%)
Systolic Blood Pressure at admission, mmHg, median (IQR) [N=331]	101 (81, 128)	105 (80, 124.5)	107 (82, 125.5)	100.5 (78, 124)
Diastolic Blood Pressure, mmHg, median (IQR) [N=284]	69 (51, 92)	70 (52, 90.2)	72 (54, 89.5)	66 (50, 91)
Pulse, beats/min, median (IQR) [N=344]	115 (97, 133)	113 (92, 132)	114 (96, 132)	113 (91.5, 131)
Fast Exam Positive, n (%) [N=252]	69 (25.9%)	179 (71.0%)	93 (73.8%)	86 (68.3%)
Hemoglobin, g/dL, median (IQR) [N=331]	12 (10, 13)	11.9 (10.1, 13.2)	11.7 (10.1, 13.3)	12.1 (10.1, 13.1)
Platelet Count, thousands, median (IQR) [N=318]	216 (165, 270)	203 (162, 256)	199 (158, 249)	212 (167, 259)
pH, median (IQR) [N=323]	7.2 (7.1, 7.3)	7.2 (7.1, 7.3)	7.2 (7.1, 7.3)	7.2 (7.1, 7.3)
Base excess, mmol/L, median (IQR) [N=314]	-8 (-12, -5)	-8 (-13.3, -3.4)	-8 (-13.0, -3.0)	-8.1 (-14.0, -4.0)
INR, median (IQR) [N=221]	1.3 (1.2, 1.5)	1.3 (1.2, 1.5)	1.2 (1.2, 1.5)	1.3 (1.2, 1.6)
TEG r-time, min [N=287]	3.9 (2.9, 4.8)	3.7 (2.8, 4.6)	3.7 (2.8, 4.4)	3.8 (3.0, 4.7)
ATC, n (%) [N=257]	50 (20.7%)	50 (19.5%)	27 (20.5%)	23 (18.4%)

GCS, Glasgow coma scale; ISS, Injury Severity Score; AIS, Abbreviated injury scale; INR, international normalized ratio; TEG, Thrombelastography. ATC represents acute traumatic coagulopathy, defined as INR ≥ 1.5 and base deficit ≥ 6 at baseline. Values are presented as median (interquartile range) unless noted. Samples sizes listed in square brackets [N] refer to the emergency laparotomy group.

Table 2

Surgical Procedures Performed During The 1st OR Visit On Patients Undergoing An Emergency Laparotomy within 90 Minutes of Arrival (E-LAP), Overall And Stratified By Treatment Group

Patients may have undergone multiple procedures, thus percentages add to greater than 100.

Procedure Type, n (%)	Overall (n=346)	1:1:1 Group (N = 174)	1:1:2 Group (N = 172)	Difference (95% CI)	P-Value
Neurosurgical procedure [/]	0 (0%)	0 (0%)	0 (0%)	0 (NA)	NA
Neck exploration	7 (2.0%)	4 (2.3%)	3 (1.7%)	0.3% (-2.6%, 3.1%)	0.86
Thoracotomy	67 (19.4%)	27 (15.5%)	40 (23.3%)	-7.4% (-15.3%, 0.4%)	0.06
Major Vascular repair	93 (26.9%)	47 (27.0%)	46 (26.7%)	0.5% (-8.8%, 9.8%)	0.91
Esophagus	1 (0.3%)	0 (0%)	1 (0.6%)	-0.6% (-1.9%, 0.6%)	0.31
Stomach	39 (11.3%)	21 (12.1%)	18 (10.5%)	2.0% (-4.4%, 8.4%)	0.55
Small intestine	92 (26.6%)	54 (31.0%)	38 (22.1%)	9.4% (0.1%, 18.7%)	0.05
Large intestine	80 (23.1%)	47 (27.0%)	33 (19.2%)	9.0% (0.4%, 17.7%)	0.04
Liver	101 (29.2%)	48 (27.6%)	53 (30.8%)	-3.5% (-13.0%, 6.0%)	0.48
Spleen	100 (28.9%)	49 (28.2%)	51 (29.7%)	-1.2% (-10.6%, 8.2%)	0.80
Kidney	43 (12.4%)	20 (11.5%)	23 (13.4%)	-2.5% (-9.4%, 4.3%)	0.47
Pancreas	26 (7.5%)	11 (6.3%)	15 (8.7%)	-2.8% (-8.1%, 2.6%)	0.31
Abdominal packing	124 (35.8%)	70 (40.2%)	54 (31.4%)	9.4% (-0.4%, 19.2%)	0.06
Temporary abdominal closure	134 (38.7%)	69 (39.7%)	65 (37.8%)	1.8% (-7.6%, 11.3%)	0.70
Pelvic procedures	8 (2.3%)	3 (1.7%)	5 (2.9%)	-1.1% (-4.2%, 2.0%)	0.47
Fracture reduction and/or fixation	13 (3.8%)	11 (6.3%)	2 (1.2%)	5.5% (1.4%, 9.6%)	0.01
Limb amputation	4 (1.2%)	2 (1.1%)	2 (1.2%)	0.0% (-2.3%, 2.2%)	0.97
Fasciotomy for compartment syndrome	11 (3.2%)	6 (3.4%)	5 (2.9%)	0.9% (-2.8%, 4.7%)	0.62
IR procedure during E-LAP	5 (1.4%)	3 (1.7%)	2 (1.2%)	1.0% (-1.6%, 3.5%)	0.45
Irrigation/debridement	42 (12.1%)	24 (13.8%)	18 (10.5)	2.8% (-3.6%, 9.2%)	0.40
Vascular shunt/thoracic packing	11 (3.2%)	4 (2.3%)	7 (4.1%)	-1.9% (-5.8%, 2.0%)	0.34

[/]Neurosurgical procedures: Craniotomy, craniectomy, subdural/epidural hematoma.

Table 3
Outcomes of Patients Who Underwent an Emergency Laparotomy within 90 Minutes of Arrival (E-LAP) By Treatment Group

The results in this table are based on the subset of 346 patients who underwent an emergency laparotomy within 90 minutes of arrival. Group differences are adjusted by site.

Outcomes	Overall (n=346)	1:1:1 (N = 174)	1:1:2 (N = 172)	Difference (95% CI)	P-Value
Survival for 3 hours, n (%)	320 (92.5)	164 (94.3)	156 (90.7)	4.2 (-1.2, 9.6)	0.13
Survival for 6 hours, n (%)	301 (87.0)	154 (88.5)	147 (85.5)	3.5 (-3.4, 10.4)	0.32
Survival for 12 hours, n (%)	298 (86.1)	152 (87.4)	146 (84.9)	2.8 (-4.2, 9.9)	0.43
Survival for 24 hours, n (%)	294 (85.0)	151 (86.8)	143 (83.1)	4.0 (-3.4, 11.3)	0.29
Survival for 72 hours, n (%)	285 (82.4)	147 (84.5)	138 (80.2)	4.8 (-3.0, 12.7)	0.23
Survival for 30 days, n (%)	267 (77.2)	138 (79.3)	129 (75.0)	4.7 (-4.1, 13.4)	0.30
Death due to Exsanguination or Hemorrhagic Shock, n (%)	52 (15.0%)	23 (13.2%)	29 (16.9%)	-4.3 (-11.6, 3.0)	0.25
Randomized RBC, mean (SD) median (IQR)	11.8 (13.1) 7 (4, 15)	9.9 (10.7) 7 (3, 12)	13.7 (15.0) 7 (4, 18)	-3.6 (-6.3, -0.8)	0.01
Randomized Plasma, mean (SD) median (IQR)	8.0 (9.4) 5 (2, 10)	9.4 (10.8) 6 (2, 12)	6.6 (7.5) 4 (2, 9)	3.0 (1.1, 4.9)	0.002
Randomized Platelets, mean (SD) median (IQR)	9.7 (9.5) 6 (6, 12)	12.7 (10.0) 12 (6, 18)	6.7 (7.9) 6 (0, 12)	6.2 (4.4, 8.1)	< 0.001
RBC at 24 hours, mean (SD) median (IQR)	15.1 (14.6) 10 (6, 19.8)	13.2 (12.7) 9 (5, 17)	17.1 (16.2) 10 (7, 21.2)	-3.5 (-6.6, -0.5)	0.02
Plasma at 24 hours, mean (SD) median (IQR)	10.4 (10.8) 7 (3, 14.8)	11.4 (11.8) 8 (3, 15.8)	9.5 (9.6) 6 (3, 13)	2.2 (-0.1, 4.4)	0.06
Platelets at 24 hours, mean (SD) median (IQR)	12.8 (12.3) 9 (6, 18)	15.0 (12.0) 12 (6, 18)	10.5 (12.2) 6 (0, 18)	4.8 (2.3, 7.3)	< 0.001
Hospital-Free Days, median (IQR)	7.9 (9.3) 0 (0, 17)	8.5 (9.6) 3.5 (0, 19)	7.4 (8.9) 0 (0, 15)	1.0 (-1.0, 2.9)	0.33
ICU-Free Days, median (IQR) ^f	6.7 (7.1) 5 (0, 11)	6.8 (7.0) 5 (0, 11)	6.6 (7.2) 5 (0, 10.5)	0.1 (-1.4, 1.6)	0.88
Ventilator-Free Days, median (IQR) ^f	9.2 (8.5) 7 (0, 15)	9.1 (8.4) 8 (0, 14)	9.2 (8.7) 7 (0, 15)	-0.1 (-1.9, 1.7)	0.90
Acute Kidney Injury, n (%)	91 (26.3%)	42 (24.1%)	49 (28.5%)	-3.5 (-12.5, 5.5)	0.45
Multi-System Organ Failure, n (%)	18 (5.2%)	11 (6.3%)	7 (4.1%)	2.8 (-1.8, 7.5)	0.24
Acute Respiratory Distress Syndrome, n (%)	41 (11.8%)	22 (12.6%)	19 (11.0%)	2.6 (-4.0, 9.1)	0.44

Outcomes	Overall (n=346)	1:1:1 (N = 174)	1:1:2 (N = 172)	Difference (95% CI)	P-Value
Disposition at 30 days, n (%)					
Home	127 (36.7%)	65 (37.4%)	62 (36.0%)	0.7 (-9.4, 10.9)	0.88
Remained hospitalized (or unknown)	92 (26.6%)	47 (27.0%)	45 (26.2%)	1.7 (-7.6, 10.9)	0.73
Morgue	79 (22.8%)	36 (20.7%)	43 (25.0%)	-4.7 (-13.4, 4.1)	0.30
Other	48 (13.9%)	26 (14.9%)	22 (12.8%)	2.3 (-5.0, 9.5)	0.54

¹ Ventilator-Free Days and ICU-Free Days were calculated based on the number of days on the ventilator or in the ICU subtracted from either the maximum follow-up of 30 days or the number of days to hospital discharge, which ever occurred first.

Table 4
Results of Cox Regression Analysis of Survival for Patients with an Emergency Laparotomy within 90 Minutes of Arrival (E-LAP)

Baseline (time 0) was set as the time of first visit to the operating room. Observations for survivors were censored at 30 days.

Variable	Hazard Ratio (95% CI)	P-Value
Treatment Group 1:1:1 (Relative to 1:1:2)	0.78 (0.50, 1.21)	0.27
Site ^I		0.74
Site B	0.61 (0.23, 1.65)	
Site C	0.50 (0.19, 1.33)	
Site D	0.73 (0.17, 3.13)	
Site E	1.02 (0.44, 2.32)	
Site F	1.38 (0.58, 3.30)	
Site G	1.58 (0.47, 5.34)	
Site H	0.71 (0.24, 2.08)	
Site I	0.85 (0.32, 2.27)	
Site J	0.55 (0.19, 1.62)	
Site K	1.20 (0.52, 2.73)	
Site L	1.11 (0.50, 2.46)	

^I Likelihood ratio test for differences between sites. Hazard ratios for individual sites are relative to site “A” as reference group.