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Transfusion of Packed Red Blood Cells is Not Associated With Improved Central Venous Oxygen Saturation or Organ Function in Patients With Septic Shock

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Abstract

Background—The exact role of packed red blood cell (PRBC) transfusion in the setting of early resuscitation in septic shock is unknown.

Study Objective—To evaluate whether PRBC transfusion is associated with improved central venous oxygen saturation (ScvO₂) or organ function in patients with severe sepsis and septic shock receiving early goal directed therapy (EGDT).

Methods—Retrospective cohort study (n=93) of patients presenting with severe sepsis or septic shock treated with EGDT.

Results—34/93 patients received at least one PRBC transfusion. The ScvO₂ goal >70% was achieved in 71.9% of the PRBC group and 66.1% of the no PRBC group (p = 0.30). There was no difference in the change in Sequential Organ Failure Assessment (SOFA) score within the first 24 hours in the PRBC group vs. the no PRBC group (8.6 to 8.3 vs. 5.8 to 5.6, P = 0.85) time to achievement of CVP >8 mmHg (732 minutes vs. 465 minutes, p = 0.14) or the use of norepinephrine to maintain MAP >65 mmHg (81.3% vs. 83.8%, p = 0.77).

Conclusions—In this study, the transfusion of PRBC was not associated with improved cellular oxygenation, as demonstrated by a lack of improved achievement of ScvO₂ >70%. Also, the transfusion of PRBC was not associated with improved organ function, or improved achievement of the other goals of EGDT. Further studies are needed to determine the impact of transfusion of PRBC within the context of early resuscitation of patients with septic shock.

Keywords

sepsis; septic shock; early goal directed therapy; packed red blood cells; transfusion

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INTRODUCTION

Sepsis is a common, lethal, and expensive health care problem. In the United States approximately 215,000 deaths are attributed to sepsis annually (1). More people die annually of sepsis than of lung and breast cancer combined. This results in over 380,000 ICU admissions yearly, and an enormous economic burden of over 17 billion dollars (1). The incidence of sepsis is estimated to be increasing steadily at 1.5% annually, with over 1.1 million cases per year by 2020 (1).

Significant improvements in mortality have been shown with an early, quantitative resuscitation strategy for those patients with severe sepsis and septic shock (2). Similar results have been reproduced by many studies, involving thousands of patients, and early goal directed therapy (EGDT) as a protocolized resuscitation strategy has been recommended by professional organizations to reduce the mortality from sepsis (3,4). The therapeutic endpoints of EGDT include maintaining a central venous pressure (CVP) of 8–12 mmHg, mean arterial pressure (MAP) \geq 65 mmHg, urine output (as marker of end organ perfusion) of \geq 0.5 co/kg/hour, and mixed venous oxygen saturation (ScvO₂) \geq 70%.

In the setting of optimized preload, packed red blood cell (PRBC) transfusion is recommended for perceived ongoing oxygen delivery (D_{O2}) versus oxygen consumption (V_{O2}) mismatch, as manifested by an ScvO₂ $<$ 70%, if the hematocrit is $<$ 30%. This is based on the physiologic rationale of anemia in the setting of potential delivery dependent oxygen consumption. Unfortunately, serious doubt has been cast on the ability of stored PRBCs to have a beneficial effect on cellular oxygenation (5–8). Due to changes occurring at the cellular level during PRBC storage, there may be equally compelling physiologic rationale to not transfuse PRBC in the early stages of septic shock. The aim of this study was to examine the association of PRBC transfusion and ScvO₂, change in organ function, as well as the achievement of the other goals of EGDT.

MATERIALS AND METHODS

This single-center retrospective cohort study was conducted in a large, urban, academic teaching hospital, with an annual Emergency Department (ED) census of approximately 56,000 patients and a 30 bed medical–surgical intensive care unit (ICU). The study protocol was approved by the local institutional review board with waiver of informed consent.

Data were collected on 93 consecutive patients who presented in septic shock and received EGDT. The trigger for EGDT at our institution is systolic blood pressure (BP) less than 90 mmHg or mean arterial pressure (MAP) less than 65 mmHg despite a crystalloid challenge of 20–30 ml/kg, or initial serum lactate concentration greater than 4 mmol/l. For the purpose of this study, patients were divided into two groups: PRBC transfusion group and no PRBC transfusion group.

We collected data on patients identified via the Surviving Sepsis Campaign Chart Review database and linked to Project IMPACT database. Primary data collection was done by two abstractors (MG and CS). CS has had extensive experience and training in database management and chart review. MG was trained in the data retrieval process prior to study initiation. Variables were defined prior to data extraction and placed in a standardized format during the data collection process. Regular meetings and monitoring of data collection were performed and the chart reviewers were blinded to study hypothesis. The following data were collected with respect to PRBC transfusion group and no PRBC transfusion group: age, gender, race, Acute Physiology and Chronic Health Evaluation (APACHE II) score, initial lactate level, estimated time to first antibiotic (measured from time to recognition of septic shock), total intravenous fluids (IVF) administered, first

vasoactive medication given, Sequential Organ Failure Assessment (SOFA) score, estimated time to central venous pressure goal (CVP 8ET), and achievement of central venous mixed oxygen saturation (SCVO₂) 70%.

The primary outcome measure was the achievement of ScvO₂ 70%. Secondary outcomes included improvement in SOFA score, achievement of CVP > 8 mmHg, and use of vasoactive medications to achieve MAP >65 mmHg. The PRBC group and no PRBC group were compared by the Pearson chi-square and Fisher's exact test to analyze statistical significance. Statistical significance was defined as $p < 0.05$.

RESULTS

A total of 93 patients were included in this study. 97% of patients in the PRBC group originated in the ED prior to ICU admission, compared with 94.9% of patients in the no PRBC group ($p = \text{NS}$). 34 patients received PRBC transfusion as part of EGDT, with an average of 4.56 units per patient early (ordered during the first 6 hours and administered within 24 hours) in their resuscitation. There were no significant differences in baseline characteristics between the two groups, except for SOFA score at time of presentation [Table 1]. Average age was 63.5 years in the PRBC group and 59.3 in the no PRBC group ($p = 0.199$). There were no significant differences in gender or race distributions. Baseline APACHE II score was 21.1 in the PRBC group and 20.3 in the no PRBC group ($p = 0.682$). Initial lactate was 6.0 and 5.4, respectively ($p = 0.463$), and initial ScvO₂ in the two groups was 66.2 and 64.3 ($p = 0.821$). There was also no significant difference in estimated time to administration of broad spectrum antibiotics, at 165 minutes for the PRBC group and 155 minutes for the no PRBC group.

Patients receiving PRBC transfusion received significantly more intravenous fluids during the initial resuscitation period of six hours, as well as over the first 72 hours of their ICU stay ($p < 0.05$). There was no difference in the use of norepinephrine to maintain MAP goal of 65 mmHg between the two groups (81.3% PRBC group vs. 83.8% no PRBC group, $p = 0.770$). There was also no difference between the PRBC group and no PRBC group with respect to improvement in organ function ($p = 0.851$)' minutes to achievement of CVP goal (732.0 vs. 465.3, $P = 0.135$), or change in ScvO₂ (4.5% vs. 3.1%, $p = 0.625$). With regard to the primary outcome, PRBC transfusion was not associated with the achievement of ScvO₂ goal (82.3% vs. 69.5%, $P = 0.301$) [Table 2].

DISCUSSION

Anemia in critical illness is common, and the majority of patients admitted to the ICU will be anemic early on in their ICU course (9–12). This is caused by a myriad of factors, including bone marrow dysfunction, erythropoietin deficiency and blunted erythropoietin response, poor nutrition, iatrogenic blood loss, and active bleeding. Anemia is normally well tolerated in healthy individuals, due to compensatory mechanisms, such as increased cardiac output and increased oxygen extraction ratio. Secondary to limited physiologic reserves, the critically ill patient typically cannot tolerate anemia as well, and published data point to worse outcomes in these patients (13–17).

Transfusion of PRBC to correct anemia seems logical, given the consequences of anemia in the setting of critical illness. Unfortunately, the great majority of clinical data states that fixing anemia with PRBC transfusion may be harmful. Consistent data regarding PRBC transfusion points to worsened clinical outcomes, such as infectious morbidity, organ dysfunction, acute respiratory distress syndrome (ARDS), mechanical ventilation, and

mortality (18–35). In the context of the limitations of these individual studies, the results consistently demonstrate that the transfusion of PRBC is not a benign intervention.

Despite these concerns, EGDT calls for an increase in hematocrit to at least 30% in the setting of perceived tissue oxygen deficit (2). With storage, PRBCs seem to lose functional and structural capability to improve that tissue oxygen deficit. There is depletion of 2,3 DPG and adenosine triphosphate (ATP), lipid peroxidation of the RBC membrane, loss of RBC deformability, and loss of normal biconcave shape (36–43). The summation of these changes leads to a red cell that is less efficient and less capable to traverse the microcirculation and offload oxygen to improve cellular bioenergetics. This is reflected in a lack of clinical data showing any improvement in the very parameters for which EGDT calls for PRBC transfusion (44–51).

The current study is congruent with the existing body of literature, and also demonstrates the inability of PRBC transfusion to improve cellular oxygenation. The initial ScvO₂ levels in this study are similar to previous data in septic patients (53–55), as well as the change in ScvO₂ associated with resuscitation (47, 56). Given the clinical data and known physiologic alterations associated with stored PRBC, our findings are not surprising and further question the rationale of transfusion in EGDT.

LIMITATIONS

The current study has several limitations. The small sample size makes drawing conclusions difficult and the retrospective design has inherent limitations. Although we capture a robust amount of data involving septic patients at our institution, we cannot exclude the possibility of unaccounted or missing data, which may cause bias and undetected differences in baseline characteristics. For example, the PRBC group received higher volumes of intravenous fluids during their resuscitation. This could be reflective of a sicker baseline in these patients, though this seems somewhat less likely given the similar APACHE scores, lactate levels, and catecholamine similarities. Also, undetected treatment differences may have existed and these differences may have affected outcome. A power analysis could not be conducted prior to the study, as the data used was what was available to the authors at the time. These facts, combined with the relatively small sample size in this trial make drawing conclusions more difficult based on this trial alone. However, our data is consistent with large, prospective trials, as well as retrospective and observational studies in this arena (5–8, 12,36,44–47,52).

CONCLUSION

In our study, the transfusion of PRBC was not associated with improvement in ScvO₂—the exact rationale for the administration of PRBCs in this clinical situation. Enough concern exists that recommending a transfusion target in septic shock patients in the acute phase of resuscitation should be revisited, as it is indeed possible that the benefits of early resuscitation of septic shock patients may be lost by a liberal transfusion threshold. To our knowledge, this is the first study to examine the effects of PRBC transfusion in the setting of EGDT. This should serve as hypothesis generating for prospective trials evaluating PRBC transfusion vs. no PRBC transfusion for patients receiving EGDT with ScvO₂ values < 70%.

References

1. Angus, Dc; Linde-Zwirble, WT.; Lidicker, J.; Clermont, G.; Carcilli, J.; Pinsky, MR. Epidemiology of severe sepsis in the United States: analysis of incidence, outcome, and associated costs of care. *Critical Care Medicine*. 2001; 29:1303–1310. [PubMed: 11445675]

2. Rivers E, Nguyen B, Havstad MA, et al. Early goal-directed therapy in the treatment of severe sepsis and septic shock. *N Engl J Med.* 2001; 345:1368–1377. [PubMed: 11794169]
3. Fuller B, Rivers E. Should Early Goal Directed Therapy Be the Standard for Sepsis? –Pro: Research Supports It. *EP Monthly.* Mar 3.2010
4. Dellinger RP, Levy MM, Carlet JM, et al. Surviving Sepsis Campaign: international guidelines for management of severe sepsis and septic shock: 2008. *Intensive Care Med.* 2008; 34:17–60. [PubMed: 18058085]
5. Marik PE, Sibbald WJ. Effect of stored-blood transfusion on oxygen delivery in patients with sepsis. *JAMA.* 1993; 269:3024–3030. [PubMed: 8501845]
6. Dietrich KA, Conrad SA, Hebert CA, Levy GL, Romero MD. Cardiovascular and metabolic response to red blood cell transfusion in critically ill volume-resuscitated nonsurgical patients. *Crit Care Med.* 1990; 18:940–944. [PubMed: 2394117]
7. Conrad SA, Dietrich KA, Hebert CA, Romero MD. Effect of red cell transfusion on oxygen consumption following fluid resuscitation in septic shock. *Circ Shock.* 1990; 31:419–429. [PubMed: 2397567]
8. Mazza BF, Machado FR, Mazza DD, Hassmann V. Evaluation of blood transfusion effects on mixed venous oxygen saturation and lactate levels in patients with SIRS/sepsis. *Clinics.* 2005; 60:311–316. [PubMed: 16138238]
9. Hebert PC, Tinmouth A, Corwin H. Controversies in RBC Transfusion in the Critically Ill. *CHEST.* 2007; 131:1583–1590. [PubMed: 17494811]
10. Corwin, HI; Parsonnet, KC.; Gettinger, A. RBC transfusion in the ICU: is there a reason? *Chest.* 1995; 108:767–771. [PubMed: 7656631]
11. Vincent, JI; Baron, J-F.; Reinhart, K., et al. Anemia and blood transfusion in critically ill patients. *JAMA.* 2002; 288:1499–1507. [PubMed: 12243637]
12. Corwin, HI; Gettinger, A.; Pearl, RG., et al. The CRIT Study: anemia and blood transfusion in the critically ill; current clinical practice in the United States. *Crit Care Med.* 2004; 32:39–52. [PubMed: 14707558]
13. Horwich TB, Fonarow GC, Hamilton MA, Maclellan WR, Borenstein J. Anemia is associated with worse symptoms, greater impairment in functional capacity and a significant increase in mortality in patients with advanced heart failure. *J Am Coll Cardiol.* 2002; 39:1780–6.
14. du Cheyron D, Pariental JJ, Fekih-Hassen M, Daubin C, Charbonneau P. Impact of anemia on outcome in critically ill patients with severe acute renal failure. *Intensive Care Med.* 2005; 31:1529–36. [PubMed: 16205892]
15. Nikolsky E, Aymong ED, Halkin A, et al. Impact of anemia in patients with acute myocardial infarction undergoing primary percutaneous coronary intervention: analysis from the controlled abciximab and device investigation to lower late angioplasty complications (CADILLAC) trial. *J Am Coll Cardiol.* 2004; 44:547–53.
16. Carson JL, Duff A, Poses RM, et al. Effects of anemia and cardiovascular disease on surgical mortality and morbidity. *Lancet.* 1996; 348:1055–60. [PubMed: 8874456]
17. Carson JL, Noveck H, Berlin JA, Gould SA. Mortality and morbidity in patients with very low postoperative hemoglobin levels who decline blood transfusion. *Transfusion.* 2002; 42:812–18. [PubMed: 12375651]
18. Taylor RW, Manganaro L, O'Brien J, Trotter SJ, Parkar N, Veremakis C. Impact of allogenic packed red blood cell transfusion on nosocomial infection rates in the critically ill patient. *Crit Care Med.* 2002; 30:2249–2254. [PubMed: 12394952]
19. Claridge JA, Sawyer RG, Schulman AM, McLemore EC, Young JS. Blood transfusions correlate with infections in trauma patients in a dose-dependent manner. *Am Surg.* 2002; 68:566–572. [PubMed: 12132734]
20. Hill GE, Frawley WH, Griffith KE, Forestner JE, Minei JP. Allogeneic blood transfusion increases the risk of postoperative bacterial infection: a meta-analysis. *J Trauma.* 2003; 54:908–914. [PubMed: 12777903]
21. Shorr AF, Jackson WL, Kelly KM, Fu M, Kollef MH. Transfusion practice and blood stream infections in critically ill patients. *Chest.* 2005; 127:1722–1728. [PubMed: 15888852]

22. El-Masri MM, Hammad TA, Fox-Wasylyshyn SM. Predicting nosocomial bloodstream infections using surrogate markers of injury severity: clinical and methodological perspectives. *Nurs Res.* 2005; 54:273–279. [PubMed: 16027570]
23. Sreeram GM, Sharma AD, Phillips-Bute B, Smith PK, Slaughter TF. Infectious complications after cardiac surgery: lack of association with fresh frozen plasma or platelet transfusions. *J Cardiothorac VaseAnesth.* 2005; 19:430–434.
24. Banbury MK, Brizzio ME, Rajeswaran J, Lytle BW, Blackstone EH. Transfusion increases the risk of postoperative infection after cardiovascular surgery. *J Am Coll Surg.* 2006; 202:131–138.
25. Rao SV, Jollis JG, Harrington RA, et al. Relationship of blood transfusion and clinical outcomes in patients with acute coronary syndromes. *JAMA.* 2004; 292:1555–1562. [PubMed: 15467057]
26. Yang X, Alexander KP, Chen AY, et al. The implications of blood transfusions for patients with non-ST-segment elevation acute coronary syndromes: results from the CRUSADE National Quality Improvement Initiative. *J Am Coll Cardiol.* 2005; 46:1490–1495.
27. Vamvakas EC, Carven JH. Allogeneic blood transfusion and postoperative duration of mechanical ventilation: effects of red cell supernatant, platelet supernatant, plasma components and total transfused fluid. *Vox Sang.* 2002; 82:141–149. [PubMed: 11952989]
28. Croce MA, Tolley EA, Coleridge JA, Fabian TC. Transfusions result in pulmonary morbidity and death after a moderate degree of injury. *J Trauma.* 2005; 59:19–23. [PubMed: 16096534]
29. Gong MN, Thompson BT, Williams P, Pothier L, Boyce PD, Christiani DC. Clinical predictors of and mortality in acute respiratory distress syndrome: potential role of red cell transfusion. *Crit Care Med.* 2005; 33:1191–1198. [PubMed: 15942330]
30. Malone DL, Dunne J, Tracy JK, Putnam AT, Scalea TM, Napolitano LM. Blood transfusion, independent of shock severity, is associated with worse outcome in trauma. *J Trauma.* 2003; 54:898–905. [PubMed: 12777902]
31. Robinson WP, Ahn J, Stiffler A, et al. Blood transfusion is an independent predictor of increased mortality in nonoperatively managed blunt hepatic and splenic injuries. *J Trauma.* 2005; 58:437–444. [PubMed: 15761334]
32. Dunne JR, Malone DL, Tracy JK, Napolitano LM. Allogenic blood transfusion in the first 24 hours after trauma is associated with increased systemic inflammatory response syndrome (SIRS) and death. *Surg Infect (Larchmt).* 2004; 5:395–404. [PubMed: 15744131]
33. Silverboard H, Aisiku I, Martin GS, Adams M, Rozycki G, Moss M. The role of acute blood transfusion in the development of acute respiratory distress syndrome in patients with severe trauma. *J Trauma.* 2005; 59:717–723. [PubMed: 16361918]
34. Dunne JR, Riddle MS, Danko J, Hayden R, Petersen K. Blood transfusion is associated with infection and increased resource utilization in combat casualties. *Am Surg.* 2006; 72:619–625. [PubMed: 16875084]
35. Palmieri TL, Caruso DM, MD, Foster KN, et al. Effect of blood transfusion on outcome after major burn injury: a multicenter study. *Crit Care Med.* 2006; 34:1602–1607. Background. [PubMed: 16607231]
36. Offner P. Age of blood: does it make a difference? *Critical Care.* 2004; 8 (Suppl):S24–S26. [PubMed: 15196318]
37. Pietersz RN, Reesink HW, de Korte D, et al. Storage of leukocyte-poor red cell concentrates: filtration in a closed system using a sterile connection device. *Vox Sang.* 1989; 57:29–36. [PubMed: 2508326]
38. Raat NJ, Verhoeven AJ, Mik EG, et al. The effect of storage time of human red cells on intestinal microcirculatory oxygenation in a rat isovolemic exchange model. *Crit Care Med.* 2005; 33:39–45. [PubMed: 15644646]
39. Valtis DJ, Kennedy AC. Defective gas-transport function of stored red blood cells. *Lancet.* 1954; 1:119–125. [PubMed: 13118742]
40. Valeri CR, Hirsh NM. Restoration *in vivo* of erythrocyte adenosine triphosphate, 2, 3-diphosphoglycerate, potassium ion, and sodium ion concentrations following the transfusion of acid-citrate-dextrose-stored human red blood cells. *J Lab Clin Med.* 1969; 73:722–733. [PubMed: 5779258]

41. Knight JA, Voorhees RP, Martin L, et al. Lipid peroxidation in stored red cells. *Transfusion*. 1992; 32:354–357. [PubMed: 1585442]
42. Card RT, Mohandas N, Perkins HA, et al. Deformability of stored red blood cells: relationship to degree of packing. *Transfusion*. 1982; 22:96–101. [PubMed: 7071924]
43. Card RT, Mohandas N, Mollison PL. Relationship of posttransfusion viability to deformability of stored red cells. *Br J Haematol*. 1983; 53:237–240. [PubMed: 6821653]
44. Marik PE, Sibbald WJ. Effect of stored-blood transfusion on oxygen delivery in patients with sepsis. *JAMA*. 1993; 269:3024–3030. [PubMed: 8501845]
45. Conrad SA, Dietrich KA, Hebert CA, Romero MD. Effect of red cell transfusion on oxygen consumption following fluid resuscitation in septic shock. *Circ Shock*. 1990; 31:419–429. [PubMed: 2397567]
46. Silverman HJ, Tuma P. Gastric tonometry in patients with sepsis: effects of dobutamine infusions and packed red blood cell transfusions. *Chest*. 1992; 102:184–188. [PubMed: 1623750]
47. Mazza BF, Machado FR, Mazza DD, Hassmann V. Evaluation of blood transfusion effects on mixed venous oxygen saturation and lactate levels in patients with SIRS/sepsis. *Clinics*. 2005; 60:311–316. [PubMed: 16138238]
48. Gilbert EM, Haupt MT, Mandanas RY, et al. The effect of fluid loading, blood transfusion, and catecholamine infusion on oxygen delivery and consumption in patients with sepsis. *Am Rev Resp Dis*. 1986; 134:873–878. [PubMed: 3777684]
49. Mink RB, Pollack MM. Effect of blood transfusion on oxygen consumption in pediatric septic shock. *Crit Care Med*. 1990; 18:1087–1091. [PubMed: 2209035]
50. Lorente JA, Landin L, dePablo R, et al. Effects of blood transfusion on oxygen transport variables in severe sepsis. *Crit Care Med*. 1993; 21:1312–1318. [PubMed: 8370294]
51. Fernandes CJ, Akamine N, DeMarco FVC, et al. Red blood cell transfusion does not increase oxygen consumption in critically ill septic patients. *Crit Care*. 2001; 5:362–367. [PubMed: 11737926]
52. Hebert PC, Wells G, Blajchman MA, et al. A multicenter, randomized, controlled clinical trial of transfusion requirements in critical care: Transfusion Requirements in Critical Care Investigators, Canadian Critical Care Trials Group. *N Engl J Med*. 1999; 340:409–417. [PubMed: 9971864]
53. Pope J, Jones A, Gaieski D, et al. Multicenter Study of Central Venous Oxygen Saturation (ScvO₂) as a Predictor of Mortality in Patients With Sepsis. *Ann Emerg Med*. 2010; 55:40–46. [PubMed: 19854541]
54. Jones A, Shapiro N, Trzeciak S, et al. Lactate Clearance Versus Central Venous Oxygen Saturation as Goals of Early Sepsis Therapy: A Randomized Controlled Trial. *JAMA*. 2010; 303 (8):739–746. [PubMed: 20179283]
55. Shapiro N, Howell M, Talmor D, et al. Implementation and outcomes of the Multiple Urgent Sepsis (MUST) protocol. *Crit Care Med*. 2006; 34:1025–1032. [PubMed: 16484890]
56. Sakr V, Chierago M, Piagnerelli M, et al. Microvascular response to red blood cell transfusion in patients with severe sepsis. *Crit Care Med*. 2007; 35:1639–1644. [PubMed: 17522571]

ARTICLE SUMMARY

1. Why is this topic important? Severe sepsis and septic shock are common, lethal, expensive, and encountered daily in the Emergency Department. Early, quantitative resuscitation strategies can significantly reduce morbidity and mortality in this setting. Unfortunately, the transfusion of PRBCs is not a benign intervention, and the ability of stored PRBCs to improve physiologic endpoints has been questioned.
2. What does this study attempt to show? This study investigates whether PRBC transfusion improves central venous oxygen saturation (the exact reason transfusion is called for during early goal directed therapy), or organ dysfunction in the setting of severe sepsis and septic shock.
3. What are the key findings? PRBC transfusion not only did not improve central venous oxygen saturation, but also failed to improve organ dysfunction, or achievement of the other end points of early goal directed therapy.
4. How is patient care impacted? The benefit of PRBC transfusion should be weighed cautiously against the potential for harm, as the ability of stored PRBCs to improve physiologic endpoints is debatable.

Table 1

Baseline characteristics

Variable	PRBC (n = 34)	No PRBC (n = 59)	P value
Age (years)	63.5	59.3	0.199
Gender			0.512
Male	22 (64.7%)	33 (55.9%)	
Female	12 (35.3%)	26 (44.1%)	
Race			0.676
Black	15 (44.1%)	22 (37.3%)	
Hispanic	3 (8.8%)	9 (15.3%)	
White	16 (47.1%)	27 (45.8%)	
Other	0(0%)	1 (1.7%)	
APACHE II	21.1	20.3	0.682
Lactate (mmol/l)	6.0	5.4	0.463
Initial SOFA score	8.6	5.8	0.003
Initial ScvO ₂ *	66.2 (11)	64.3 (12)	0.821

* Values represent the mean (SD)

Table 2

Resuscitation variables

Variable	PRBC (<i>n</i> = 34)	No PRBC (<i>n</i> = 59)	Pvalue
Intravenous fluids* (l)			
0–6 hours	5.7	3.9	<0.05
6–72 hours	17.6	13.0	<0.05
Total	23.3	16.9	<0.05
Norepinephrine for MAP >65 mmHg	26 (81.3%)	31 (83.8%)	0.770
Δ SOFA Score (24 hours)	0.22	0.19	0.851
CVP > 8** (minutes)	732.0	465.3	0.135
SCVO ₂ 70%**	28 (82.3%)	41 (69.5%)	0.301
Δ SCVO ₂ , %***	4.5 (9)	3.1 (8)	0.625

* All patients were resuscitated with isotonic crystalloid. A total of 7 patients received albumin as well.

** Measured from time that EGDT protocol began.

*** Values represent the mean change (SD)