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Goal-directed Resuscitative Interventions during Pediatric Interfacility Transport

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Abstract

Background and Objectives—This manuscript reports results of the first NIH-funded prospective interfacility transport study, to determine the effect of goal-directed therapy administered by a specialized pediatric team to critically ill children with the Systemic Inflammatory Response Syndrome (SIRS). We hypothesized that goal-directed therapy during interfacility transport would decrease hospital length of stay, prevent multiple organ dysfunction, and reduce subsequent ICU interventions.

Methods—Prospective data was collected on all pediatric interfacility transport patients with SIRS transported by the Angel One Transport team at Arkansas Children's Hospital. A 10 month data collection period was followed by institution of a goal-directed resuscitation protocol. Data was subsequently collected for 10 additional months followed by comparison of pre and post-

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Contributors' Statement Page

Michael H Stroud: Dr. Stroud conceptually designed this study, secured funding, and was responsible for the day to day progress of the study. He drafted the initial manuscript and approved the final manuscript as submitted.

Ronald C Sanders: Dr. Sanders helped with drafting the manuscript, contributed to all editing, and approved the final manuscript as submitted.

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Janice E Sullivan: Dr. Sullivan helped with study design and contributed to drafting and editing of the manuscript. She approved the final manuscript as submitted.

Parthak Prodhan: Dr. Prodhan helped with study design and contributed to drafting and editing of the manuscript. He approved the final manuscript as submitted.

Maria Melguizo-Castro: Maria designed the data collection instruments, oversaw data collection, conducting statistical analyses, critically reviewed the manuscript, and approved the final manuscript as submitted.

Todd Nick: Dr. Nick oversaw all aspects of study design and statistical analyses, critically reviewed the manuscript, and approved the final manuscript as submitted.

intervention groups. All transport personnel underwent training with didactics and high-fidelity simulation until mastery with goal-directed resuscitation was achieved.

Results—All transport patients were screened for SIRS using established parameters, and 235 (123 pre-intervention; 112 post-intervention) were enrolled. Univariate analysis revealed shorter hospital stay (11 ± 15 vs. 7 ± 10 days; $p=0.02$) and fewer required therapeutic ICU interventions in the post-intervention group (TISS-28 scores: 19.4 ± 6.8 vs. 17.3 ; $p=0.04$). ICU stay and incidence of organ dysfunction were not statistically different. Multi-variable analysis showed a 1.6 day (95% CI: 1.3–2.03; $p=0.02$) decrease in hospital stay in the post-intervention group.

Conclusions and Relevance—This study suggests that goal-directed therapy administered by a specialized pediatric transport team has the potential to impact the outcomes of critically ill children. Findings from this study should be confirmed across multiple institutions, but have the potential to impact the clinical outcomes of critically ill children with SIRS.

Keywords

interfacility transport; goal directed therapy; shock; sepsis; SIRS

Introduction

The practice of pediatric interfacility transport has changed in recent years. Improvements in equipment, transport vehicles, therapeutic interventions, and education have afforded teams the opportunity to deliver critical care in the field. Recent evidence has shown that specialized teams with such capabilities can impact the outcomes of critically ill children¹, and current consensus guidelines recommend the use of specialized teams for transport of critically ill children². Evidence has shown that improved monitoring techniques may also impact the care provided during transport³. Specialized pediatric transport teams are becoming mobile intensive care units (ICU) capable of delivering state-of-the-art ICU-level interventions at referring facilities and during transport. Timely intervention is necessary to optimize the outcomes of critically ill children during transport.

Goal-directed therapy has been instrumental in improving the outcomes of adults and children with severe sepsis and septic shock^{4–6}. Systemic Inflammatory Response Syndrome (SIRS) is a precursor to severe sepsis and septic shock. This constellation of clinical findings was developed by a joint consensus conference by the American College of Chest Physicians and the Society of Critical Care Medicine to describe the complex host response to insult from a myriad of conditions including infection⁷. Pediatric SIRS criteria were subsequently developed and include age adjusted normative values for temperature, heart rate, respiratory rate, and white blood cell count⁸. Randomized trials in adult and pediatric transport patients have shown improved outcomes with increased use of out-of-hospital interventions^{3,9}. Although goal-directed therapy has become common practice in academic institutions, this approach has not been widely used outside tertiary care centers¹⁰. We hypothesized that the institution of goal-directed therapy by a specialized pediatric transport team during interfacility transport would improve the outcomes of critically ill patients with SIRS and SIRS-induced shock.

Methods

This clinical trial was registered with [ClinicalTrials.gov](https://clinicaltrials.gov) prior to patient enrollment (NCT 01293500) and was funded by the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD 1R21HD060171-02A). A prospective, single center, controlled before-and-after study compared study groups prior to and after institution of a goal-directed resuscitation protocol for transport of critically ill patients with SIRS and SIRS-induced shock. The study was approved by the University of Arkansas for Medical Sciences Institutional Review Board, which waived the need for informed consent. In lieu of informed consent, an informational sheet describing the study was provided to parents on arrival of the transport team at each outside facility.

Preliminary data was collected on all transport patients meeting inclusion/exclusion criteria over a 10 month period. Demographic data was collected as well as data for illness severity, hospital length of stay (LOS), ICU LOS, incidence of multiple organ dysfunction syndrome (MODS), need for therapeutic ICU interventions, and mortality. The Pediatric Logistic Organ Dysfunction (PELOD) Scoring System was used to estimate the incidence of MODS. PELOD scores have been validated as a reliable measure of MODS in critically ill children^{11,12}. The Therapeutic Intervention Scoring System-28 (TISS-28) scores were collected as an indicator of needed ICU interventions. TISS-28 scores are validated for use in pediatric patients and are commonly used in clinical studies as a measure of therapeutic interventions in critically ill children^{13,14}. These scores are also used as a measure of needed bedside nursing time with one point on the TISS-28 scale equivalent to 10.6 minutes of each eight hour shift.

Following initial data collection, goal-directed protocolized resuscitation of patients with SIRS was instituted. All transport personnel were educated on the use of goal-directed resuscitation over a 6 week period via lectures and case scenarios using high-fidelity simulation, until mastery was achieved. Following this period of teaching, transport patients with SIRS and SIRS-induced shock were resuscitated using this approach (FIGURE 1). Data was collected over a second 10 month period followed by comparison of pre and post intervention groups. Care provided by outside facilities was not standardized in either group. All transport calls were taken by board-certified pediatric critical care physicians who provided suggested interventions based on perceived patient acuity.

Selection and Description of Participants

Consecutive pediatric patients aged one month to seventeen years meeting age-adjusted SIRS criteria were enrolled. All patients were interfacility transports by the Angel One Transport team from outside referring facility emergency departments to Arkansas Children's Hospital (ACH). The Angel One Transport team is a specialized pediatric interfacility transport team based at ACH, servicing the entire state of Arkansas and surrounding states. Transport team personnel included a registered respiratory therapist, registered nurse, and resident (PGY-2 or higher) or fellow-level (Pediatric Critical Care or Pediatric Emergency Medicine) physician, all with critical care experience. Patients were defined as having SIRS if they met previously published consensus criteria⁸. Patients were excluded for any of the following: 1) known or suspected congenital heart disease, 2) known

or suspected cardiomyopathy or myocarditis, 3) diabetic ketoacidosis (DKA), 4) traumatic brain injury, 5) burn injury, or 6) known or suspected active hemorrhage.

The primary outcome was to determine if institution of goal-directed therapy during interfacility pediatric transport reduced hospital LOS for critically ill pediatric patients with SIRS or SIRS-induced shock. Secondary outcomes included reduction in ICU LOS, incidence of MODS, and need for therapeutic ICU interventions. Additionally, cerebral oxygenation numbers obtained by means of Near Infrared Spectroscopy (NIRS) were collected on a convenience sample of patients among both groups, to determine if this methodology can be used as a resuscitation guide during transport of critically ill pediatric patients with SIRS and SIRS-induced shock.

Statistical Methods

Multivariable linear model analyses using ordinary least squares (OLS) were used for the analysis of hospital LOS and ICU LOS¹⁵. Models were adjusted for covariates: gender, race, age, and Pediatric Index of Mortality II (PIM2) score. Restricted cubic splines were fit for PIM2 score and transport time.

For the secondary outcome, reduced incidence of MODS as measured by the PELOD score, repeated measures mixed model analyses were used. This modeling strategy allows handling correlations between repeated measures taken on the same child; additionally, it is adapted to situations where the number of observations differs by participant¹⁶. The correlation structure used to describe correlations among repeated measures was compound symmetry, and the Kenward-Roger approximation to the degrees of freedom was used. The response variable was the PELOD score, and covariates included first PELOD score, PIM2 score, gender, race, intervention period, ICU days, and the interactions between intervention days/First PELOD, and intervention days/predicted death. Three way interactions between days, intervention period and PIM2; days, first PELOD and intervention period; as well as the other two way interactions were investigated but excluded. The final model selected was the random intercept and slope model in which each participant is allowed to have its own regression line. This model was selected as the best fit over the random intercept only model based on the likelihood ratio test.

The reduction in TISS-28 score during ICU stay was investigated using repeated measures mixed model analyses, in a similar way as described for the PELOD analysis. Covariates included first TISS-28 score, PIM2 score, gender, race, intervention period, ICU days, and the interactions between intervention days/first TISS-28 score, and days/predicted death. Three way interactions between days, intervention period and PIM2; days, first TISS-28 and intervention period; as well as the other two way interactions were investigated but excluded. The final model selected is the random intercept and slope model in which each participant is allowed to have its own regression line. This model was selected because the random intercept only model did not converge.

Descriptive statistics and multivariable linear model analyses were performed using statistical software R version 2.15 (Vienna, Austria)¹⁷ and the rms package¹⁸. SAS Version

9.3 (SAS institute Cary, NC) was used for the mixed model analyses. All tests performed were two sided, and P-values <0.05 were considered statistically significant.

Power Calculation

Sample size was calculated prior to study initiation. We estimated that at least 83 patients needed to be enrolled per intervention period in order to detect a 2 day reduction in hospital LOS. This sample size was based on a two-sided t-test with $\alpha=0.05$ and 90% power, assuming a common standard deviation. Preliminary data available before study initiation showed a mean hospital LOS for pediatric SIRS patients of 8.55 ± 3.47 days (mean $\pm$ SD). For this sample size calculation, the 80% upper limit of the confidence interval for the standard deviation was used, giving an estimate of 3.94 for standard deviation.

Results

There were 242 eligible transport encounters during the study period, corresponding to 235 unique patients. Seven patients had two different transport encounters. Each transport encounter was considered an independent observation for modeling purposes, so the sample size studied was 242 participant-encounters, with 127 observations in the pre intervention period and 115 in the post-intervention period.

Demographic and clinical characteristics of the study participants were similar at baseline (Table 1). There were no significant differences for baseline characteristics except transport time (pre-intervention 94 ± 34 minutes vs. post-intervention 85 ± 31 minutes; $p=0.04$) and for the outcome hospital LOS (pre-intervention 11 ± 15 days vs. post-intervention 7 ± 10 days; $p=0.02$). Statistical differences were addressed using two-sample t-tests for continuous variables and a fisher's exact test for categorical variables. For modeling purposes, other and Hispanic races were combined.

Transport Interventions

The amount of fluid resuscitation given during transport was not significantly different before and after protocol implementation (pre-intervention 15.9 ± 15.4 ml/kg vs. post-intervention 16.1 ± 20.2 ml/kg; $p=0.46$). All subjects received at least maintenance IV fluids during transport. For those patients with >10% predicted mortality (PIM-II) there was a trend toward enhanced fluid resuscitation (pre-intervention 15.9 ± 15.3 ml/kg vs. post-intervention 41.1 ± 41.5 ml/kg; $p=0.09$) following protocol implementation. Six subjects in the post-intervention group received inotropic support (dopamine titrated to 10mcg/kg/min or epinephrine at 0.1mcg/kg/min) administered through a peripheral IV catheter.

Hospital Length of Stay

There was a significant reduction of hospital LOS ($p=0.02$) in the post-intervention group. On average, patients in the post-intervention period spent 3.5 less days in the hospital after adjusting for covariates (95%CI 0.02 to 6.9 days). Normality assumptions could not be met secondary to the wide range of LOS, so a log transformation was investigated. The log transformed model showed a significant effect of intervention period on hospital LOS

($p=0.03$). On average, patients in the post-intervention period spent 1.6 less days in the hospital after adjusting for covariates (95%CI 1.3 to 2.03 days).

ICU Length of Stay

There appeared to be a trend toward reduced ICU LOS in the post-intervention group with an estimated effect of 2.1 days (95%CI -0.4 to 4.7 days). However, this difference was not statistically significant ($p=0.08$). A log transformation was also explored to assess differences for ICU LOS; however, the effect of intervention on ICU LOS remained non-significant ($p=0.21$).

Incidence of Multiple Organ Dysfunction Syndrome (MODS)

PELOD scores were calculated daily for all patients in the ICU. Results of mixed models indicated a decline in PELOD scores during ICU stay (Figure 2), dependent on the first PELOD score [Estimate (β)= -0.59 , Standard Error (S.E.)= 0.04 , $p<0.001$], and on PIM2 score ($\beta=2.03$, S.E= 0.98 , $p=0.04$). Additionally, PELOD scores overall were lower in the post-intervention period ($\beta = 1.03$, S.E= 0.55 , $p=0.06$), but rate of decline between pre and post PELOD scores was not significantly different ($\beta=0.07$, S.E= 0.22 , $p=0.75$).

Needed Therapeutic Interventions

Mean first TISS-28 scores were lower in the post intervention group (17.3 ± 6.6 vs 19.4 ± 6.8 , $p=0.04$). Results of mixed models indicated a decline in TISS-28 scores during ICU stay (Figure 3), dependent on the first TISS-28 Score ($\beta=-0.04$, S.E= 0.01 , $p=0.002$).

Cerebral Oxygenation

Cerebral oxygenation monitoring using NIRS (Near-Infrared Spectroscopy) technology was conducted on a convenience sample ($N=39$; 20 pre, 19 post) of patients. The NIRS device used was the INVOS™ 5100C monitoring device by Covidien Ltd (Colorado, USA). A single probe was placed on the center of the forehead. NIRS saturations using this method have been shown to trend with invasive monitoring of tissue oxygen delivery¹⁹. Somatic monitoring was not used in the present study. Previous research suggests these numbers may not adequately reflect tissue oxygen delivery in patients over 10 kg ²¹. Subjects less than 10 kg were monitored with a neonatal/infant sized probe. All others were monitored with a standard sized probe. The use of NIRS monitoring during pediatric interfacility transport has previously been shown to be effective during transport of patients via helicopter²⁰. Monitoring commenced after arrival of the transport team at the outside facility and continued until arrival at the receiving facility. Subjects in the goal-directed therapy group had statistically higher cerebral oxygenation numbers on average than those in the pre-intervention group (71 ± 18 vs. 66 ± 14 ; $p<0.05$).

Discussion

The present study is the first to provide evidence that use of goal-directed therapy by specialized pediatric transport teams in the field improves the outcomes of critically ill children. Previous retrospective data has shown that transport of critically ill pediatric patients by specialized pediatric transport teams result in fewer complications and improved

outcomes¹. Goal-directed therapy has been instrumental in improving outcomes of critically ill patients with sepsis and septic shock⁴⁻⁶. Rapid deployment of specialized teams capable of delivering state-of-the-art critical care may be more beneficial than rapid delivery of critically ill patients to tertiary care centers. Specialized pediatric transport teams should be armed with evidence-based interventions, capable of being delivered to critically ill patients prior to and during interfacility transport.

In the present study, subjects in the goal-directed therapy group had a shorter length of hospital stay than those not receiving protocolized goal-directed therapy. The protocol (FIGURE 1) used in this study was constructed based on the current best available evidence for resuscitation and treatment of pediatric patients with severe sepsis and septic shock⁶. Prior to institution of protocolized resuscitation, patients were treated based on suggested interventions by medical control physicians, one of ten board certified pediatric intensivists. These guidelines call for interventions aimed at enhancing tissue oxygen delivery in the face of increased tissue oxygen demand. These early interventions include rapid intravenous fluid resuscitation, early administration of inotropic agents via peripheral IV, and correction of electrolyte abnormalities including abnormal serum glucose and calcium levels. These interventions were accomplished in the goal-directed therapy group in the present study. Additionally during transport, pulse oximetry was maintained >95%, continuous vital signs were measured, oscillometric blood pressure readings were obtained every 3-5 minutes, and threshold age-adjusted heart rates were maintained with continued fluid resuscitation in route. Subjects did not receive significantly different amounts of fluid resuscitation based on group assignment [15.91 ± 15.35 ml/kg (pre) vs. 16.13 ± 20.17 ml/kg (post); $p=0.46$]. All subjects received at least maintenance IV fluids, and subjects in the post-intervention group. This held true with all patients regardless of initially severity of illness. Subjects in the goal-directed therapy group with PIM2 scores >10% did show a trend toward enhanced amounts of fluid resuscitation that was not statistically significant [15.91 ± 15.35 ml/kg (pre) vs. 41.05 ± 41.52 ml/kg (post; $p=0.09$)]. Six subjects (all in the goal-directed therapy group) received peripherally administered inotropic agents during transport. It is likely that a combination of factors leading to overall improved quality of care and enhanced tissue oxygen delivery during transport led to the observed outcome differences.

Subjects in the goal-directed therapy group required fewer initial ICU interventions, as evidenced by lower TISS-28 scores. Additionally, they had lower PELOD scores and a trend toward shorter ICU LOS, though the present study was not powered to detect such a difference. These differences were seen despite similar initial PIM2 scores, further suggesting the importance of rapid and appropriate interventions during interfacility transport. Though PELOD scores were different, the rates of decline after ICU admission were similar in both groups, emphasizing the need for continued ICU care and suggesting that patients in the goal-directed therapy group were more adequately resuscitated on ICU arrival. Overall mortality was 2% (2 pre; 3 post).

Cerebral oxygenation monitoring using NIRS technology was conducted on a convenience sample of patients in this study. Cerebral oxygenation numbers have been shown to trend with invasive measures of mixed venous saturation (SVO_2)¹⁹. SVO_2 numbers are a direct reflection of adequacy of tissue oxygen delivery, but currently require invasive ICU

monitoring. Cerebral oxygenation monitoring is a non-invasive tool with the potential for use as a guide for resuscitation prior to ICU arrival. Subjects in the goal-directed therapy group had statistically higher cerebral oxygenation numbers during transport than those in the control group (71 ± 18 vs. 66 ± 14 ; $p < 0.05$). Though this difference may not be clinically significant, future studies should evaluate the potential of this non-invasive tissue oxygen delivery monitoring tool to guide resuscitative interventions during interfacility transport.

Limitations of the current study include its single center nature and before-and-after intervention design. The Angel One Transport team at ACH is a specialized pediatric interfacility transport team with a composition similar to other specialized interfacility transport teams across the country, except for physician presence on the ACH team during the study period. Physicians were present during both pre and post-intervention periods. The team has conducted other clinical trials in the out-of-hospital setting^{3,20}. The method of resuscitation used in this study would be easy to institute among specialized pediatric transport teams at other institutions. The before-and-after design of this study lends itself to the possibility of overall improved care during the study period. Though we realize this limitation, randomization after teaching goal-directed resuscitation to the team was not possible. In addition, the non-normative distribution of the LOS data may have overestimated the benefit of goal-directed therapy. The findings of this study should be confirmed across other institutions, but suggest that improved care delivered by specialized pediatric interfacility transport teams has the potential to impact the clinical outcomes of critically ill children with SIRS.

Conclusion

Specialized pediatric transport teams have evolved into mobile intensive care units capable of delivering definitive care to critically ill children during interfacility transport. Arming these teams with goal-directed therapeutic protocols has the potential to impact the outcomes of critically ill children. Continued research efforts should seek to develop evidence-based therapies to be administered by specialized pediatric transport teams in the field, prior to tertiary care center arrival. In addition, training outside facility healthcare providers in goal-directed therapy may further improve care for these children.

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Abbreviations

ACH	Arkansas Children's Hospital
DKA	Diabetic Ketoacidosis
ICU	Intensive Care Unit
LOS	Length of Stay
MODS	Multiple Organ Dysfunction Syndrome
NIRS	Near-Infrared Spectroscopy
PELOD	Pediatric Logistic Organ Dysfunction
PIM-II	Pediatric Index of Mortality II
SIRS	Systemic Inflammatory Response Syndrome
TISS-28	Therapeutic Intervention Scoring System

References

- Orr RA, Felmet KA, Han Y, et al. Pediatric specialized transport teams are associated with improved outcomes. *Pediatrics*. 2009; 124(1):40–8. [PubMed: 19564281]
- Stroud MH, Trautman MS, Meyer K, et al. Pediatric and neonatal interfacility transport: results from a national consensus conference. *Pediatrics*. 2013; 132(2):359–66. [PubMed: 23821698]
- Stroud MH, Prodhon P, Moss M, Fiser R, Schexnayder S, Anand K. Enhanced monitoring improves pediatric transport outcomes: a randomized controlled trial. *Pediatrics*. 2011; 127(1):42–8. [PubMed: 21173006]
- Rivers E, Nguyen B, Havstad S, et al. Early goal-directed therapy in the treatment of severe sepsis and septic shock. *N Engl J Med*. 2001; 345:1368–77. [PubMed: 11794169]
- Dellinger RP, Levy MM, Rhodes A, et al. Surviving sepsis campaign: international guidelines for management of severe sepsis and septic shock, 2012. *Intensive Care Med*. 2013; 39(2):165–228. [PubMed: 23361625]
- Brierley J, Carcillo JA, Choong K, et al. Clinical practice parameters for hemodynamic support of pediatric and neonatal septic shock: 2007 update from the American College of Critical Care Medicine. *Crit Care Med*. 2009; 37(2):666–88. [PubMed: 19325359]
- Balk RA. Systemic inflammatory response syndrome (SIRS): Where did it come from and is it still relevant today? *Virulence*. 2014; 5(1):20–26. [PubMed: 24280933]
- Goldstein B, Giroir B, Randolph A, et al. International pediatric sepsis consensus conference: definitions for sepsis and organ dysfunction in pediatrics. *Pediatr Crit Care Med*. 2005; 6(1):2–8. [PubMed: 15636651]
- Stiell IG, Wells GA, Field B, et al. Advanced life support for out of hospital respiratory distress. *N Engl J Med*. 2007; 356(21):2156–64. [PubMed: 17522399]
- Ninis N, Phillips C, Bailey L, et al. The role of healthcare delivery in the outcome of meningococcal disease in children: case-control study of fatal and non-fatal cases. *BMJ*. 2005; 330(7506):1475. [PubMed: 15976421]
- Leteurtre S, Martinot A, Duhamel A, et al. Development of a pediatric multiple organ dysfunction score: use of two strategies. *Med Decis Making*. 1999; 19:399–410. [PubMed: 10520678]
- Leteurtre S, Martinot A, Duhamel A, et al. Validation of the pediatric logistic organ dysfunction (PELOD) score: prospective, observational, multicenter study. *Lancet*. 2003; 362:192–197. [PubMed: 12885479]
- Miranda DR, de Rijk A, Schaufeli W. Simplified therapeutic intervention scoring system: the TISS-28 items: results from a multicenter study. *Crit Care Med*. 1996; 24:67–73.

14. Yeh TH, Pollack MM, Holbrook PR, Fields AI, Ruttiman U. Assessment of pediatric intensive care – application of the therapeutic intervention scoring system. *Crit Care Med.* 1982; 10(8):497–500. [PubMed: 7094595]
15. Harrell FE Jr, Lee KL, Mark DB. Multivariable prognostic models: issues in developing models, evaluating assumptions and adequacy, and measuring and reducing errors. *Stat Med.* 1996; 15:361–87. [PubMed: 8668867]
16. Doig CJ, Zygun DA, Fick GH, et al. Study of clinical course of organ dysfunction in intensive care. *Crit Care Med.* 2004; 32:384–90. [PubMed: 14758152]
17. R Core Team. R: A language and environment for statistical computing. R Foundation for Statistical Computing; Vienna, Austria: 2012. ISBN 3-900051-07-0, <http://www.R-project.org/>
18. Harrell, FE, Jr. Rms: regression modeling strategies. R package version 3.4-0. 2012. <http://CRAN.R-project.org/package=rms>
19. Bhutta AT, Ford JW, Parker JG, et al. Noninvasive cerebral oximeter as a surrogate for mixed venous saturation in children. *Pediatr Cardiol.* 2007; 28(1):34–41. [PubMed: 17219027]
20. Stroud MH, Gupta P, Prodhan P. Effect of altitude on cerebral oxygenation during pediatric interfacility transport. *Pediatr Emerg Care.* 2012; 28:329–32. [PubMed: 22453725]
21. Ortmann LA, Fontenot EE, Seib PM, Eble BK, Bhutta AT. Use of near-infrared spectroscopy for estimation of renal oxygenation in children with heart disease. *Pediatr Cardiol.* 2011; 32(6):748–53. [PubMed: 21445607]

Figure 1. Transport Goal-directed Therapy Protocol

Figure 2. Estimated PELOD Score according to intervention period. Shaded areas indicate 95% confidence bands

Figure 3. Estimated TISS-28 Score according to intervention period. Shaded areas indicate 95% confidence bands.

Table 1

Demographic and Clinical Characteristics of Study Participants

	N	Pre-Intervention (N=123)	Post-Intervention (N=112)	P Value
Gender	235			0.7
<i>Female</i>		47 (38%)	46 (41%)	
<i>Male</i>		76 (62%)	66 (59%)	
Race	235			0.6
<i>Black</i>		20 (16%)	17 (15%)	
<i>White</i>		83 (67%)	75 (67%)	
<i>Hispanic</i>		17 (14%)	13 (12%)	
<i>Other</i>		3 (2%)	7 (6%)	
Age (Years)	235	5.2 ± 5.5	4.7 ± 4.9	0.4
Transport Duration (minutes)	235	94 ± 34	85 ± 31	0.04
Inotropic Support		0	6	0.01
Fluid Resuscitation (ml/kg)		15.9±15.4	16.1±20.2	0.46
PIM-2 >10%		15.9±15.3	41.1±41.5	0.09
In-Hospital Mortality	235			0.7
<i>No</i>		121 (98%)	109 (97%)	
<i>Yes</i>		2 (2%)	3 (3%)	
Hospital Length of Stay (Days)	235	11 ± 15	7 ± 10	0.02
Post-Transport ICU admission	235			0.1
<i>No</i>		34 (28%)	43 (38%)	
<i>Yes</i>		89 (72%)	69 (62%)	
ICU Length of Stay (Days)	158	6 ± 9	4 ± 5	0.08
% Total Admitted to ICU		72%	62%	0.08
PIM2 Score	235	0.08±0.22	0.10± 0.26	0.6
First PELOD Score^λ	164	8.3 ± 7.1	7.8 ± 9.4	0.67
First TISS28 Score^λ	164	19.4 ± 6.8	17.3 ± 6.6	0.04

N is the number of non-missing values, numbers in parenthesis are percentages.

x ± s represents the mean ± Standard Deviation.

Statistical differences were addressed using two-sample t-tests for continuous variables and a fisher's exact test for categorical variables.

^λSix patients went to the ICU two times. For the mixed models, these events are treated as independent events.