Adherence to PALS Sepsis Guidelines and Hospital Length of Stay

AUTHORS: Raina Paul, MD,[a] Mark I. Neuman, MD, MPH,[a] Michael C. Monuteaux, ScD,[a] and Elliot Melendez, MD[a,b]

[a]*Division of Emergency Medicine, and* [b]*Medicine Critical Care Program, Boston Children's Hospital, Boston, Massachusetts*

KEY WORDS

sepsis, septic shock, PALS, adherence, guidelines

ABBREVIATIONS

ED—emergency department
EMR—electronic medical record
IQR—interquartile range
IV—intravenous
IVF—intravenous fluids
LOS—length of stay
PALS—Pediatric Advanced Life Support
PIM2—Pediatric Index of Mortality Score, version 2
SS—severe sepsis and septic shock

Drs Paul, Melendez, and Neuman conceived the study, designed the study, and supervised the conduct of the trial and data collection. Dr Paul undertook acquisition of data of included patients and managed the data, including quality control; drafted the manuscript; and takes responsibility for the article as a whole. Dr Monuteaux provided statistical advice on study design and analyzed the data. All authors contributed substantially to the article's revision.

www.pediatrics.org/cgi/doi/10.1542/peds.2012-0094

doi:10.1542/peds.2012-0094

Accepted for publication Mar 27, 2012

This work was previously presented at the Pediatric Academic Society Meeting, Emergency Medicine Section; April 29–May 4, 2011; Denver, CO.

Address correspondence to Raina Paul, MD, Division of Emergency Medicine, Children's Hospital, 300 Longwood Ave, Boston, MA 02115. E-mail: raina.paul@childrens.harvard.edu

PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

Copyright © 2012 by the American Academy of Pediatrics

FINANCIAL DISCLOSURE: *The authors have indicated they have no financial relationships relevant to this article to disclose.*

FUNDING: No external funding.

WHAT'S KNOWN ON THIS SUBJECT: Adherence to Pediatric Advanced Life Support resuscitation guidelines for children with sepsis is low; however, few studies have been conducted in the tertiary care emergency department setting.

WHAT THIS STUDY ADDS: Adherence to septic shock guidelines in a tertiary care pediatric emergency department is low. Adherence to fluid guidelines and the entire PALS algorithm was associated with a shorter hospital length of stay.

abstract

BACKGROUND AND OBJECTIVES: Few studies have evaluated sepsis guideline adherence in a tertiary pediatric emergency department setting. We sought to evaluate (1) adherence to 2006 Pediatric Advanced Life Support guidelines for severe sepsis and septic shock (SS), (2) barriers to adherence, and (3) hospital length of stay (LOS) contingent on guideline adherence.

METHODS: Prospective cohort study of children presenting to a large urban academic pediatric emergency department with SS. Adherence to 5 algorithmic time-specific goals was reviewed: early recognition of SS, obtaining vascular access, administering intravenous fluids, delivery of vasopressors for fluid refractory shock, and antibiotic administration. Adherence to each time-defined goal and adherence to all 5 components as a bundle were reviewed. A detailed electronic medical record analysis evaluated adherence barriers. The association between guideline adherence and hospital LOS was evaluated by using multivariate negative binomial regression.

RESULTS: A total of 126 patients had severe sepsis (14%) or septic shock (86%). The median age was 9 years (interquartile range, 3–16). There was a 37% and 35% adherence rate to fluid and inotrope guidelines, respectively. Nineteen percent adhered to the 5-component bundle. Patients who received 60 mL/kg of intravenous fluids within 60 minutes had a 57% shorter hospital LOS ($P = .039$) than children who did not. Complete bundle adherence resulted in a 57% shorter hospital LOS ($P = .009$).

CONCLUSIONS: Overall adherence to Pediatric Advanced Life Support sepsis guidelines was low; however, when patients were managed within the guideline's recommendations, patients had significantly shorter duration of hospitalization. *Pediatrics* 2012;130:e273–e280

Severe sepsis and septic shock (SS) in children is associated with a high overall mortality of 10.6% and is higher in those with chronic illness (12%).[1,2] In 2006, formal resuscitation guidelines for SS were revised and disseminated through the Pediatric Advanced Life Support (PALS) program by the American Heart Association (Fig 1).[3–5] The major components of the most recent 2010 guidelines do not vary from the 2006 recommendations.[5] Based on the proposed algorithm by Carcillo et al through the American College of Critical Care Medicine practice parameter, PALS ideally recommends 60 mL/kg of intravenous fluids (IVFs) within 15 minutes of meeting the definition of SS, although administration within 60 minutes has been suggested as adequate resuscitation.[4,6,7] Other recommendations include timely recognition and vascular access within 5 minutes, antibiotic delivery within 60 minutes, and initiation of vasoactive agents at 60 minutes (which should be used peripherally until central access is obtained) (Fig 1).[4,8,9]

A critical component of the guideline includes early fluid resuscitation, which in adults is associated with decreased mortality.[10] Pediatric studies have also been conducted in the community, intensive care, and international settings, and have shown that timely fluid resuscitation is associated with decreased mortality and functional morbidity.[11–14] Few studies addressing guideline adherence within a tertiary care emergency department (ED) have been conducted, however. Carcillo and colleagues[12] comment that community hospitals often do not have the benefit of tertiary care centers, where children with shock are met by an organized team approach with providers dedicated to specific patient care tasks. Although this team approach exists for trauma patients in shock, the same cannot be assumed for those with SS.

There have been 2 studies conducted in a tertiary care ED evaluating adherence to PALS sepsis guidelines. These institutions demonstrated poor adherence to fluids, vasoactive agents, and antibiotics and demonstrated some improvement in these parameters after quality improvement interventions.[15,16] These studies did not, however, evaluate all time points within the PALS algorithm, including recognition and vascular access. Additionally, they did not evaluate the specific PALS recommendation to complete 60 mL/kg of IVFs within 60 minutes, but rather evaluated time to initiation of the first 20 mL/kg bolus.[15,16] Therefore, we evaluated the adherence to the entire PALS guideline as a bundle, as well as specific components to understand barriers to adherence and assess whether following the guideline's time-specific parameters is associated with shorter hospital and ICU length of stay (LOS).

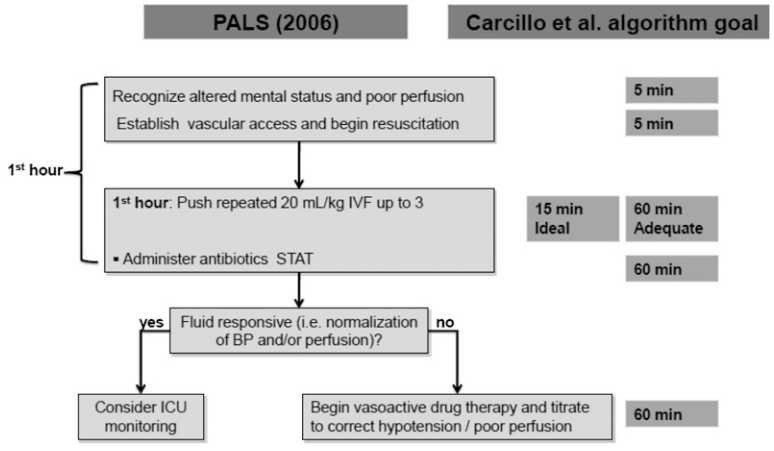

FIGURE 1
Five time points evaluated for adherence from 2006 PALS algorithm. (Adapted from Carcillo JA, Fields AI; American College of Critical Care Medicine Task Force Committee Members. Clinical practice parameters for hemodynamic support of pediatric and neonatal patients in septic shock. *Crit Care Med.* 2002;30 [6]:1370.)[6]

METHODS

Study Design and Setting

We evaluated adherence to the 2006 PALS septic shock algorithm (Fig 1).[4] We enrolled consecutive patients presenting to our pediatric ED who met the definition of SS between November 2009 and March 2011. The study was conducted in a pediatric tertiary care hospital with an ED volume of ~58 000 visits per year.

Selection of Participants

Each week, patients who met our case definition of SS were retrospectively identified for guideline adherence. Patients were identified by reviewing all children who were evaluated in the ED and admitted to any critical care, step-down, oncology, or bone marrow transplant unit. In our institution, most patients with SS are hospitalized in 1 of these locations. Patients were classified as having either severe sepsis or septic shock by using definitions cited from the 2005 international pediatric sepsis consensus conference.[17] By using this definition, severe sepsis is considered if sepsis is present, plus the presence of acute respiratory distress syndrome alone or 2 or more other organ dysfunctions (pulmonary, neurologic, hematologic, renal, or hepatic).[17] Septic shock exists if sepsis is present, plus cardiovascular organ dysfunction specifically. The electronic medical record (EMR) was then reviewed for provider guideline adherence and was performed by the primary investigator (R.P.) in addition to a pediatric

intensivist (E.M.) if ambiguity existed. We excluded patients with structural congenital heart disease with residual physiologic dysfunction, renal failure, diabetic ketoacidosis, sickle cell disease, severe anemia, and those with a do not resuscitate directive.

Evaluation of Adherence to Guidelines

We reviewed the EMR to evaluate adherence to the 5 main components of the PALS algorithm (Fig 1).[4] Compliance with guidelines was determined for each step of the algorithm. Adherence to the entire algorithm bundle (either all 5 components or 4 components if inotropes were not indicated) was also documented.

Our initial time point was defined as the time when the patient first met our case definition of SS and was used as the starting time from which the 5 other time intervals were calculated. This initial time point was determined from documentation available in the EMR. Most study patients met criteria for SS based on initial hemodynamic compromise; however, some patients met the definition only with the addition of abnormal laboratory parameters indicating organ dysfunction. For these latter patients, the time point used for meeting the definition included the time when laboratories were resulted and posted in the EMR. Time to recognition was determined by documentation of severity of illness, transfer to an ED resuscitation room, additional intravenous (IV) placement, or second fluid bolus initiation. Time to IV access was also abstracted from the EMR, as it is documented as part of routine nursing practice. Time to completion of 60 mL/kg of IVFs, time to initiation of inotropes if needed, and time to antibiotics were abstracted from documentation in the medication administration record. Administration of 60 mL/kg of IVFs within 15 minutes was regarded as perfect adherence, although as 60 minutes has been recommended as adequate resuscitation, we used this as our goal adherence time.[4,7] Adherence to vasoactive agents was considered only if indicated, that is, if hypotension persisted after 60 mL/kg of IVFs were administered.[16] Of note, if IV access was obtained and fluids were given, before definition or recognition of SS, these times were considered as 0 minutes from definition; no negative numbers were calculated. We also evaluated adherence to each component of the algorithm over time, as well as the bundle over time, by using a p-chart with standard statistical process control methods. A p-chart is a type of statistical process control chart that depicts the proportion of nonconforming units in subgroups of varying sizes.

It is institutional practice to have a documenting nurse for critical care patients. To evaluate the accuracy of the aforementioned documentation, 10 patients underwent real-time provider documentation of these 5 time points as sepsis resuscitation occurred. Time points noted by prospective data collection were within 5 minutes of those times documented in the EMR.

Barriers to Adherence

We identified barriers to adherence through a detailed analysis by using the EMR. The components of the algorithm bundle that had the poorest adherence were further analyzed, including fluid delivery. Factors that could pertain to inadequate administration of fluids, such as a delay in the previous steps of recognition and vascular access, were explored. The fluid delivery devices used for each patient were analyzed from the EMR. We also evaluated specific laboratory tests that were obtained (specifically creatinine, liver function tests, lactic acid, and coagulation profiles), as abnormalities in these values can be used to identify organ dysfunction and define severe sepsis.

Relationship Between Adherence to Guidelines and LOS

Based on previous publications, hospital and ICU LOS for this population approximates a negative binomial distribution, and average LOS has been demonstrated to be on average 8.7 days.[18] A sample size of 70 would be needed to demonstrate a 50% shorter hospital LOS with guideline adherence, by using a 2-sided P value with an α level of significance of 0.05, a power of 90%, and a Poisson distribution (approximating a negative binomial distribution). We determined if poor fluid and algorithm bundle adherence (as dichotomous variables) were associated with hospital and ICU LOS (continuous variables) by using multivariate negative binomial regression while adjusting for severity of illness, by using the Pediatric Index of Mortality Score, version 2 (PIM2) and other comorbidities as listed in Table 1.[19] The PIM2 is a validated measure used to depict severity of illness in critically ill children at presentation as opposed to later in a patient's course.[19] Additionally, the PIM2 has been used in other studies as a marker of severity of illness in children with SS.[14] Additional covariates (age, gender, time of presentation) were eligible for inclusion in the multivariate model if they were significantly associated with our outcome in univariate testing at the $P < .05$ level. Our final model included only PIM2 score and other comorbidities, as other demographic characteristics were not significant on univariate analyses.

The Statistical Package for the Social Sciences version 18.0 (SPSS Inc, Chicago, IL) and Stata version 11 (StataCorp, College Station, TX) were used for statistical analysis. Statistical process control charts were created by using Microsoft Excel 2010 (Seattle, WA). This study was approved by the hospital's institutional review board.

RESULTS

During the 16-month study period, 126 patients met criteria for severe sepsis

TABLE 1 Demographics of Study Population

Patient Characteristic	*n* (%); (*n* = 126)
Male	68 (54)
Type of sepsis	
Septic shock	108 (86.5)
Severe sepsis	18 (14.3)
Age in years (median [IQR])	9.2 (3–16)
<1 y	15 (11.9)
Mortality	6 (4.8)
Comorbidities	75 (60)
Hematologic malignancy	8 (6.3)[a]
Solid tumor malignancy	7 (5.6)[a]
Bone marrow transplantation	5 (4.0)[a]
Solid organ transplantation	5 (4.0)[a]
Short gut	11 (8.7)[a]
Immunosuppression from chronic therapy (Crohn disease, rheumatoid arthritis)	15 (11.9)[a]
Neurodegenerative disorder	5 (4)[a]
Other	25 (19.8)[a]
PIM2 score (mean [SD])	10.3 (12.9)
Intubated/noninvasive ventilation in ED	26 (20.6)
Vasopressor administered	58 (46)
Dopamine	52 (41.3)
Epinephrine	4 (3.17)
Norepinephrine	1 (0.79)
Catecholamine refractory shock	20 (15.9)
Indwelling vascular catheter	33 (26.2)
Central venous catheter placement in ED	30 (23.8)
Intraosseous placement in ED	10 (7.9)

[a] Do not add up to 60% because of overlapping comorbidities.

(14%) or septic shock (86%) (Table 1). The median age was 9 years (interquartile range [IQR], 3–16) and 54% were male patients. Comorbidities existed in 60% of patients, the mean PIM2 score was 10.3 (± SD 12.9), and 5% died. Forty-six percent had an identified pathogen or infectious process (Supplemental Table 4). Fifty-four (43%) patients met the definition of SS immediately on presentation. The remaining 72 patients (58%) progressed to SS during their ED stay.

Adherence

Adherence to the 5 components of the PALS algorithm are detailed in Fig 2. Ninety-nine patients (79%) were recognized within 5 minutes of meeting the SS criteria. Eighty-five patients (67%) had IV access within 5 minutes of definition. Forty-six children (37%) had adequate IVF adherence, receiving 60 mL/kg of IVFs within 60 minutes. Fourteen children (11%) had perfect IVF adherence, receiving 60 mL/kg within 15 minutes. Median time to administration of 60 mL/kg of IVFs was 83 minutes (IQR, 43–145). All patients received normal saline, which is conventionally used for resuscitation in our ED. Of the 47% with fluid refractory shock, 35% received an inotrope at 60 minutes from definition, with a median time to administration of 90 minutes (IQR 51–164). Eighty-eight patients (70%) received an antibiotic within 60 minutes. Perfect adherence to the algorithm bundle was observed for 19% of patients. Additionally, it was noted that 4 patients (3.2%) had hypocalcemia and 0% of these had correction within the recommended 60 minutes of meeting the definition. Two patients (1.6%) had hypoglycemia and 100% of these had correction within the recommended 60 minutes.

Barriers From EMR

Analysis of recognition and vascular access steps preceding IVF delivery were examined to determine if these factors contributed to lack of adherence to fluid administration goals, as IVFs cannot be delivered without meeting these preceding steps. Figure 3 depicts the adherence steps from definition, to recognition, to IV placement, and then IVF administration. The uppermost branch of the figure demonstrates prompt recognition and IV access in most patients (58.7%, *n* = 74). Despite this, of these patients who adhered to both these steps, only 28.5% (*n* = 36) received 60 mL/kg of fluid within 60 minutes. On the contrary, the lowest branch demonstrates that in the minority of patients where there was not timely recognition or IV access (12%, *n* = 15), there were no patients with adequate fluid delivery.

An IV infusion pump versus a pressure bag, rapid infuser, or manual push-pull system was used in 49% of cases. Laboratory testing used to define patients as having SS was not consistently obtained. Coagulation profiles were obtained in 28% of children, liver function tests in 50%, and lactic acid in 66%.

Statistical process control charts demonstrated no improvement in care over time (Fig 4). Of the 5 algorithm time points analyzed over time, adherence to fluids closely paralleled overall bundle adherence with high variability in process throughout the study period (Fig 5).

Relationship Between Adherence to Guidelines and LOS

Patients who adhered to fluid guidelines and the algorithm bundle had a significantly shorter hospital and ICU LOS (Tables 2 and 3). Adjusting for PIM2 score on presentation, patients who received 60 mL/kg of IVFs within 60 minutes had a 57% shorter hospital LOS (*P* = .039) and a 42% shorter ICU LOS (*P* = .024) than children with inadequate fluid delivery. Additionally, adherence to all 5 algorithm steps as a bundle resulted in a 57% shorter hospital LOS (*P* = .009) and a 59% shorter ICU LOS (*P* = .035).

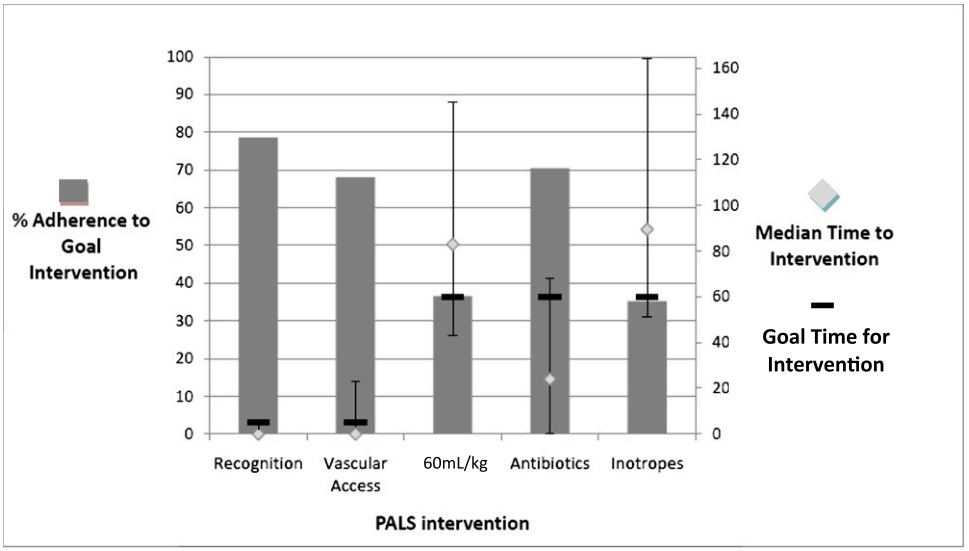

FIGURE 2
Percent adherence to 5 algorithm time points and median time to intervention (with goal time displayed). *Error bars represent IQRs for median times.

DISCUSSION

We have demonstrated that adherence to 2006 PALS septic shock guidelines in our tertiary care ED is inadequate, especially for fluid and inotrope delivery. Poor fluid adherence has also been demonstrated in community-based EDs where adherence to PALS guidelines was observed in only 30% of patients.[11] This study observed a reduction in mortality from 38% to 8% with good fluid adherence. In another study of children transferred to a tertiary care institution, early fluid resuscitation was associated with lower mortality (9% vs 15%) and functional morbidity (1% vs 4%).[12] An international study also demonstrated low rates of adherence to fluid guidelines with 38% adherence to 2002 American College of Critical Care Medicine guidelines in a UK pre-PICU setting.[13] The entry point for this study, however, was once a patient was identified as ill enough to need transport to a tertiary care center; the first critical hours of resuscitation were not directly analyzed.

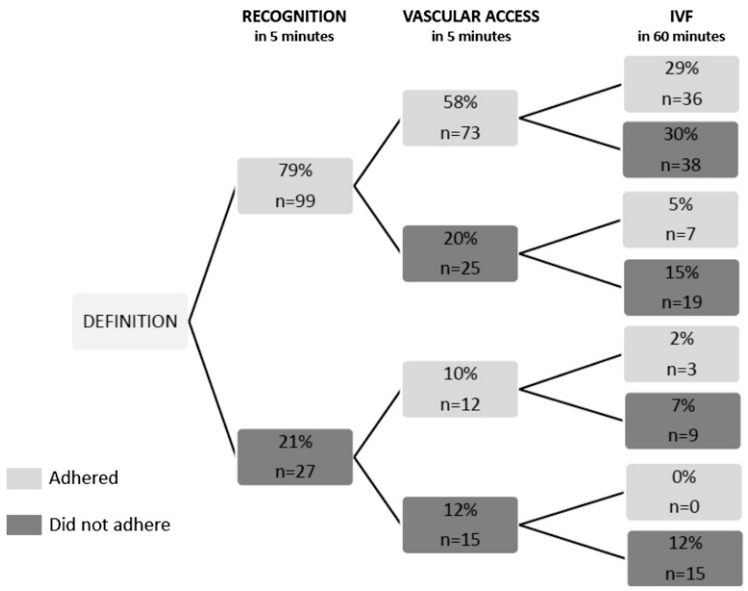

FIGURE 3
Percentage adhering to the recognition, vascular access, and IVF administration goal times, as dependent on the preceding algorithm step. *Uppermost branch*: In most patients there was adherence to recognition and vascular access goals (59%). Despite this, only 29% met IVF adherence goals. *Lowest branch*: In a minority of patients there was nonadherence to recognition and vascular access goals (12%), with untimely recognition and IV access; 0% met fluid goals in this subset.

Our study demonstrates that despite increased resources and personnel in a tertiary care setting, there is still a deficiency in the care for children with SS. Although previous investigations in an academic setting achieved more timely fluid and inotrope delivery after a quality improvement intervention, they failed to meet specific PALS goals, including delivery of 60 mL/kg of IVFs within 60 minutes.[15,16] Furthermore, studies examining all 5 time points within the algorithm as a bundle have not been conducted.

Suboptimal fluid delivery was not related to delayed recognition and vascular access. Even with prompt recognition and vascular access in most patients, only a minority of these patients went on to receive 60 mL/kg of IVFs within

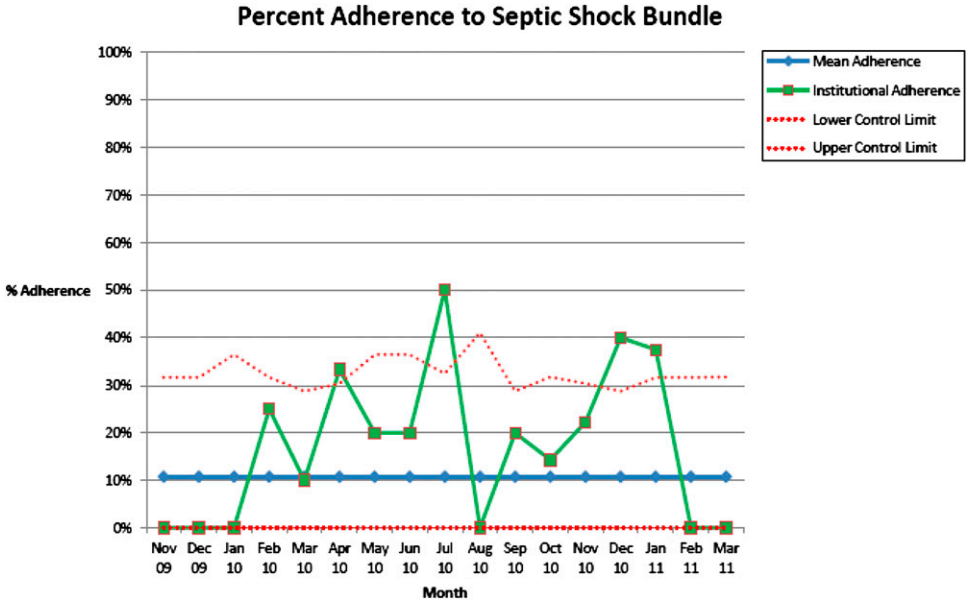

FIGURE 4

Adherence to PALS algorithm bundle over entire study period. Mean adherence, mean percentage adhering to guidelines over study period; Institutional adherence, percent adherence at our institution each month over the study period; Lower and Upper control limit, calculated by using an α of 0.05.

60 minutes. This suggests that IV placement or recognition alone do not account for fluid nonadherence, but rather something inherent to fluid delivery itself. The lack of timely IVF administration can be attributed to either a lack of knowledge regarding PALS recommendations or the inability to administer fluid quickly. Evidence for the latter may be supported by the use of an IV pump for fluid delivery in 49% of study subjects. Stoner et al[20] demonstrated that because the maximum rate for an infusion pump is typically 999 mL/h, the administration of 60 mL/kg within 60 minutes can be achieved only for children weighing $<$16 kg.

Although using the correct fluid delivery device is pivotal, prompt recognition and adequate vascular access are also necessary. In the small percentage of patients

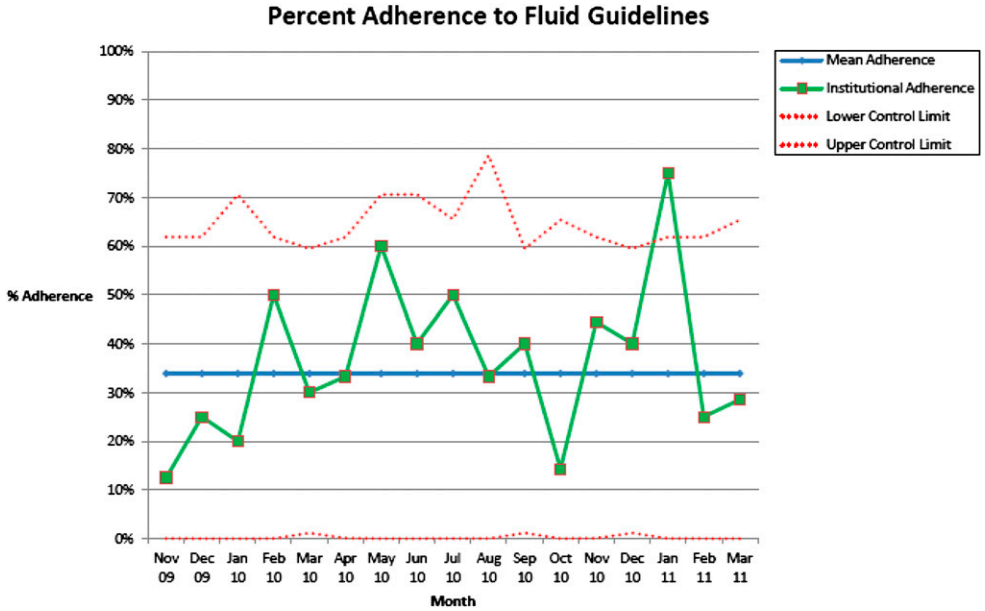

FIGURE 5

Adherence to PALS fluid guidelines over entire study period. Mean adherence, mean percentage adhering to guidelines over the study period; Institutional adherence, percent adherence at our institution each month over the study period; Lower and Upper control limit, calculated by using an α of 0.05.

TABLE 2 Association of Fluid Adherence With LOS

	Fluid Adherence, $n = 46$, Mean No. Days[a]	Fluid Nonadherence, $n = 80$, Mean No. Days[a]	Decrease, %	*P* Value[b]
Hospital LOS	8	11.2	57	.039
ICU LOS	5.5	7.2	42	.024

[a] Unadjusted means.

[b] *P* value references "percent decrease in LOS" by using negative binomial regression, adjusting for PIM2 score at presentation and other comorbidities.

who did not have timely recognition or vascular access, it was not feasible to then deliver 60 mL/kg of IVFs within 60 minutes for any patient. Therefore, although using the appropriate device for fluid delivery is critical to bundle adherence and was the most problematic for our cohort, recognition and vascular access are also crucial steps.

By graphing each algorithm step over time by using statistical process control charts, we noted that fluid adherence closely paralleled the poor overall bundle adherence. This further lends credence to the fact that this step was the driving factor leading to poor overall bundle adherence.

A minority of patients met the definition of SS on arrival. Despite this, recognition of progression of disease during the ED stay was not problematic for most patients. This does, however, highlight the need for continuous monitoring of children with systemic inflammatory response syndrome and sepsis, as deterioration is common. Recognition of severe sepsis, however, requires subtle parameters, such as coagulation profiles, liver function tests, and lactic acid, which can be the first indicator of organ dysfunction. Despite this, these were obtained in few patients, possibly owing to provider lack of knowledge regarding their value in assessing the pediatric patient. Most patients in our cohort had septic shock and it is possible that those with severe sepsis went unrecognized.

We observed a significant decrease in hospital and ICU LOS in those patients who had timely fluid delivery and adherence to the total algorithm bundle. Although not directly measured in our study, it is likely that appropriate resuscitation resulted in earlier correction of shock state, thus decreasing LOS. In addition to improved patient care, this decrease in hospitalization likely has significant cost implications. This is the first study to analyze all the major components of the PALS algorithm in relation to meaningful clinical outcomes and supports their use as a bundle. Other parameters often used in assessment of goal-directed resuscitation were not measured, including lactate clearance and central venous saturation. Although these were often obtained once the patient was admitted to the ICU or step-down unit, they were rarely performed while in the ED. A lactic acid was obtained in only 66% of patients in the ED, and then obtained at inconsistent intervals thereafter in the ICU. As such, the determination of lactate clearance would be unrepresentative of the entire cohort and would be confounded by the additional therapies received in the ICU. Additionally, despite placement of a central venous catheter in 23% of patients in the ED, central venous saturation was not obtained in any patient and thus it was not analyzed as an outcome. Finally, cardiac index is not routinely measured in our ED.

TABLE 3 Association of Total Algorithm Adherence With LOS

	Algorithm Bundle Adherence, $n = 24$, Mean No. Days[a]	Algorithm Bundle Nonadherence, $n = 102$, Mean No. Days[a]	Decrease, %	*P* Value[b]
Hospital LOS	6.8	10.9	57	.009
ICU LOS	5.5	6.8	59	.035

[a] Unadjusted means.

[b] *P* value references "percent decrease in LOS" by using negative binomial regression, adjusting for PIM2 score at presentation and other comorbidities.

A quality improvement intervention is currently being undertaken to improve adherence to PALS guidelines in our institution. To have a sustainable intervention that uses fewer resources, our extensive review of barriers will allow us to focus on improvement of fluid delivery as a method to increase bundle compliance.

One of the major strengths of our study lies in the setting in which it was conducted: an ED within an academic children's hospital without limited resources. This strength also serves as a limitation in that our finding may not be generalizable to smaller, nonacademic medical centers. Information obtained through retrospective review of the medical record may be subject to documentation bias. There is, however, often a documenting nurse at the bedside specifically for these patients, allowing for more accurate documentation. Given that we used specific definitions of SS rather than more-inclusive clinical judgment, our study cohort likely excluded those who were on the less severe spectrum of illness. Additionally, patients were eligible for inclusion through screening of ICU and step-down logs. It was thus possible that some patients recovered from severe sepsis while in the ED and were admitted to a non-ICU setting and would not have been captured by our review. Finally, as providers were aware of this study, it may have increased their adherence to the guidelines. Our monthly analysis of adherence over time, however, demonstrates no consistent statistical change in adherence throughout the study period, indicating that the

Hawthorne effect did not play a major role in our findings.

CONCLUSIONS

Adherence to PALS guidelines for patients with SS was suboptimal at the study institution. Adherence to delivery of 60 mL/kg of IVFs within 60 minutes and initiation of inotropic support within 60 minutes was especially low. When care matched the guideline's time-defined interventions, patient outcomes were improved, as evidenced by shorter hospital and ICU LOS.

ACKNOWLEDGMENT

We thank Richard Bachur, MD, for his critical review of the manuscript.

REFERENCES

1. Watson RS, Carcillo JA, Linde-Zwirble WT, Clermont G, Lidicker J, Angus DC. The epidemiology of severe sepsis in children in the United States. *Am J Respir Crit Care Med*. 2003;167(5):695–701
2. Carcillo JA. Pediatric septic shock and multiple organ failure. *Crit Care Clin*. 2003; 19(3):413–440, viii
3. Zaritzky AL, Nadkarni VM, Hickey RW, et al. *Pediatric Advanced Life Support Manual*. Dallas, TX: American Heart Association; 2002
4. Ralston M, Hazinski MF, Zaritsky AL, et al. *Pediatric Advanced Life Support Manual*. American Heart Association; 2006
5. Kleinman ME, Chameides L, Schexnayder SM, et al. Part 14: pediatric advanced life support: 2010 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. *Circulation*. 2010; 122(18 suppl 3):S876–S908
6. Carcillo JA, Fields AI; American College of Critical Care Medicine Task Force Committee Members. Clinical practice parameters for hemodynamic support of pediatric and neonatal patients in septic shock. *Crit Care Med*. 2002;30(6):1365–1378
7. Parker MM, Hazelzet JA, Carcillo JA. Pediatric considerations. *Crit Care Med*. 2004; 32(suppl 11):S591–S594
8. 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 [published correction appears in *Crit Care Med*. 2009;37(4):1536]. *Crit Care Med*. 2009; 37(2):666–688
9. Melendez E, Bachur R. Advances in the emergency management of pediatric sepsis. *Curr Opin Pediatr*. 2006;18(3):245–253
10. Rivers E, Nguyen B, Havstad S, et al; Early Goal-Directed Therapy Collaborative Group. Early goal-directed therapy in the treatment of severe sepsis and septic shock. *N Engl J Med*. 2001;345(19):1368–1377
11. Han YY, Carcillo JA, Dragotta MA, et al. Early reversal of pediatric-neonatal septic shock by community physicians is associated with improved outcome. *Pediatrics*. 2003; 112(4):793–799
12. Carcillo JA, Kuch BA, Han YY, et al. Mortality and functional morbidity after use of PALS/APLS by community physicians. *Pediatrics*. 2009;124(2):500–508
13. Inwald DP, Tasker RC, Peters MJ, Nadel S; Paediatric Intensive Care Society Study Group (PICS-SG). Emergency management of children with severe sepsis in the United Kingdom: the results of the Paediatric Intensive Care Society sepsis audit. *Arch Dis Child*. 2009;94(5):348–353
14. Oliveira CF, Nogueira de Sá FR, Oliveira DS, et al. Time- and fluid-sensitive resuscitation for hemodynamic support of children in septic shock: barriers to the implementation of the American College of Critical Care Medicine/Pediatric Advanced Life Support Guidelines in a pediatric intensive care unit in a developing world. *Pediatr Emerg Care*. 2008;24(12):810–815
15. Cruz AT, Perry AM, Williams EA, et al. Implementation of goal-directed therapy for children with suspected sepsis in the emergency department. *Pediatrics*. 2011;127(3). Available at: www.pediatrics.org/cgi/content/full/127/3/e758
16. Larsen GY, Mecham N, Greenberg R. An emergency department septic shock protocol and care guideline for children initiated at triage. *Pediatrics*. 2011;127(6). Available at: www.pediatrics.org/cgi/content/full/127/6/e1585
17. Goldstein B, Giroir B, Randolph A; International Consensus Conference on Pediatric Sepsis. International pediatric sepsis consensus conference: definitions for sepsis and organ dysfunction in pediatrics. *Pediatr Crit Care Med*. 2005;6(1):2–8
18. Odetola FO, Gebremariam A, Freed GL. Patient and hospital correlates of clinical outcomes and resource utilization in severe pediatric sepsis. *Pediatrics*. 2007;119(3):487–494
19. Slater A, Shann F, Pearson G; Paediatric Index of Mortality (PIM) Study Group. PIM2: a revised version of the Paediatric Index of Mortality. *Intensive Care Med*. 2003;29(2): 278–285
20. Stoner MJ, Goodman DG, Cohen DM, Fernandez SA, Hall MW. Rapid fluid resuscitation in pediatrics: testing the American College of Critical Care Medicine guideline. *Ann Emerg Med*. 2007;50(5):601–607