Timing of Opioid Administration as a Quality Indicator for Pain Crises in Sickle Cell Disease

Melissa D. Mathias, MD[a], Timothy L. McCavit, MD, MS[b,c]

abstract

BACKGROUND AND OBJECTIVE: Time to opioid administration (TTO) has been suggested as a quality of care measure for sickle cell disease patients with vaso-occlusive crisis (VOC). We sought to determine whether TTO was associated with outcomes of emergency department (ED) visits for VOC.

METHODS: We conducted a single-center retrospective cohort study of ED visits for VOC. The primary outcome was hospital admission, with secondary outcomes of change between the first 2 pain scores, area under the curve (AUC) for pain scores at 4 hours (pain score AUC), total ED length of stay, and total intravenous opioids. In both univariate and multivariate analyses, mixed regression (logistic for admission, linear for secondary outcome variables) was used to evaluate association of TTO with outcome.

RESULTS: In 177 subjects, 414 ED visits for VOC were identified. Inpatient admission occurred in 53% of visits. The median TTO for admitted patients was 86 minutes vs 87 minutes for those not admitted. TTO was not associated with inpatient admission in either univariate or multivariate analyses. In multivariate analyses with secondary outcomes, decreased TTO was associated with greater improvement between the first 2 pain scores, decreased pain score AUC, decreased total ED length of stay, and increased total opioids.

CONCLUSIONS: Although TTO was not associated with admission, it was independently associated with 4 important secondary outcomes: change in initial pain scores, pain score AUC, total ED length of stay, and total intravenous opioids. The association of a process measure, TTO, with these outcomes encourages the institution of TTO reduction efforts in the ED.

[a]*Department of Pediatrics, Memorial Sloan-Kettering Cancer Center, New York, New York;* [b]*Division of Hematology-Oncology, Department of Pediatrics, University of Texas Southwestern Medical Center at Dallas, Dallas, Texas; and* [c]*Center for Cancer and Blood Disorders, Children's Medical Center Dallas, Dallas, Texas*

Dr Mathias designed the data collection instrument, collected the data, and drafted the initial manuscript; Dr McCavit conceptualized and designed the study, collected and analyzed the data, and drafted and revised the manuscript; and both authors approved the final manuscript as submitted.

www.pediatrics.org/cgi/doi/10.1542/peds.2014-2874

DOI: 10.1542/peds.2014-2874

Accepted for publication Dec 17, 2014

Address correspondence to Timothy L. McCavit, MD, U.T. Southwestern Medical Center, 5323 Harry Hines Blvd, Dallas, TX 75390-9063. E-mail: tim.mccavit@childrens.com

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

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

FUNDING: Funded by CTSA grant UL1-RR024982.

POTENTIAL CONFLICT OF INTEREST: Dr McCavit has consulted for Glycomimetics and Pfizer in the developmental of a novel therapy for sickle cell pain; Dr Mathias has indicated she has no potential conflicts of interest to disclose.

WHAT'S KNOWN ON THIS SUBJECT: Patients with sickle cell disease frequently express dissatisfaction with emergency department treatment of painful crises. Time to opioid administration has been suggested as a quality of care measure for painful crises.

WHAT THIS STUDY ADDS: Although not associated with hospital admission, time to opioid administration in sickle cell disease painful crises was associated with secondary outcomes including improvement between the first 2 pain scores, decreased pain score area under the curve at 4 hours, decreased emergency department length of stay, and increased total opioids.

The acute painful episode or vaso-occlusive crisis (VOC) is the clinical hallmark of sickle cell disease (SCD). VOC accounts for many of the 113 000 annual hospitalizations in the US and is the most common reason for hospitalization in both children and adults with SCD.[1–3] These admissions result in high costs for the medical system and the individual patient.[4] Children with SCD frequently have pain after discharge and accordingly miss multiple days of school, contributing to diminished academic achievement.[4] Additionally, caregivers of SCD patients with VOC miss days of work, which may adversely affect the socioeconomic status of patient families. Unfortunately, the management of VOC, consisting primarily of opioids, anti-inflammatory medication, and intravenous hydration, has not changed in decades.[5–8] Recent studies of novel agents for VOC treatment, including inhaled nitric oxide and purified poloxamer-188, demonstrated little or no clinical benefit.[9,10]

Although some centers in larger cities have established "day hospitals" for the specialized care of SCD patients with VOC,[11] the vast majority of initial medical care occurs in hospital emergency departments (EDs). In both the ED and the inpatient setting, both patients and parents report a high level of dissatisfaction with VOC treatment, including delays in receiving treatment and undertreatment of pain.[12,13] Patients with SCD and their families also rate their in-hospital care as of lower quality than race- and age-matched controls.[14,15] In an effort to define and ultimately improve the quality of care (QOC) for children with SCD, novel QOC measures were recently proposed.[16] These measures were evaluated for both the quality of supporting evidence and their perceived clinical importance. Among 41 proposed quality indicators, 4 received the highest importance rating of 9 on a 10-point scale. Two of these 4 indicators pertained to the treatment of VOC: (1) receipt of parenteral analgesic within 60 minutes of registration or 30 minutes of triage, and (2) initial pain assessment performed using an age-appropriate scale and repeated within 30 minutes of initial analgesic dosing. These measures are consistent with other measures in the ED wherein the timeliness of interventions is associated with improved QOC and outcomes.[17] Unfortunately, both of these measures had the lowest level of supporting evidence (descriptive studies and/or expert opinion). Therefore, we aimed to study a single center's SCD population with VOC to determine whether the time to opioid administration (TTO) was associated with outcomes of care in the ED. We hypothesized that increased TTO would be associated with worse patient outcomes, including increased likelihood of inpatient admission.

METHODS

Study Design

This retrospective cohort study was of TTO in children with VOC who received parenteral opioids in the ED of Children's Medical Center Dallas. The Institutional Review Board of the University of Texas Southwestern Medical Center approved the study and waived the requirement for informed consent.

Subject Identification

Subjects were identified for inclusion in the cohort by query of administrative records from our center. First, all ED encounters for SCD patients between January 1, 2008, and December 31, 2010, were identified by using *International Classification of Diseases, Ninth Revision, Clinical Modification* codes for SCD (282.41, 282.42, and 282.6*x*) as either primary or secondary diagnosis. To this list of encounters, the eligibility criteria were applied to create the final cohort. Inclusion criteria were (1) previously established diagnosis of SCD (any genotype); (2) presence of VOC defined as the new onset of pain for which there is no explanation other than vaso-occlusion[1]; (3) age $\geq$5 and $\leq$18 years; and (4) treatment with parenteral opioids. Children under 5 years of age were not included owing to concern that the differentiation of VOC from other sources of pain can be difficult in this age group. Exclusion criteria were (1) confounding sources of pain (eg, headache and cholelithiasis); (2) transfer to the ED from other medical centers; (3) any surgical procedure within 2 weeks of presentation; (4) simple transfusion in the preceding 30 days; and (5) participation in a chronic transfusion program within the preceding 6 months.

Outcome Variables

The primary outcome variable was hospital admission. Secondary outcomes included (1) change in first 2 recorded pain scores (defined as pain score 1 minus pain score 2); (2) area under the curve (AUC) for all pain scores at 4 hours (pain score AUC)[18]; (3) total ED length of stay in minutes; and (4) total intravenous opioid dose received in milligrams per kilogram of morphine equivalent.[19] Our center routinely uses either a 5-point patient-reported numeric pain scale or the 5-point Faces pain scale for assessment of pain intensity. For pain score AUC, pain scores were graphed as a function of time for the first 4 hours of the ED visit. The pain score AUC serves as a quantitative representation of the total amount of pain experienced by the patient.[18]

Predictor Variable

TTO was defined as the time in minutes from presentation to ED (either triage or registration, whichever was first) to receipt of the first dose of parenteral opioids. TTO was analyzed in minutes, as both a continuous variable and categorized in quartiles.

Covariates

Relevant covariates were collected, including patient age (analyzed as both a continuous and categorical variable); initial dose of opioid and total opioids received (both converted to morphine equivalents[19]); gender; presence of fever; baseline hemoglobin and baseline reticulocyte count (baseline defined as a rolling average of the past 3 values from sickle cell clinic visits as documented in our center's sickle cell database); hemoglobin and reticulocyte count at presentation to the ED; primary payer; arrival by ambulance; number of previous admissions for VOC in the preceding 12 months; number of missed clinic visits in the preceding 12 months; pain location; number of pain locations; weekend presentation; and year of presentation. Additionally, our ED instituted the routine use of an electronic medical record (EMR) on May 29, 2009, nearly in the middle of our study frame, so we included a variable to indicate before or after EMR initiation. Because of the retrospective nature of this study, data summarizing the provision of therapies before the hospital visit were unavailable. Recommended outpatient VOC care in our center included oral hydration, local analgesia with applied heat (eg, heating pad), and a medication regimen consisting of alternating ibuprofen with an oral opioid (typically a combination of acetaminophen with codeine or hydrocodone).

Study Procedures

Data were manually extracted from the EMR onto case report forms before entry into a Redcap database.[20] To assess the accuracy of data entry by the first author, the senior author reviewed 20 charts independently. The agreement between authors was 97%, so no further double chart review was performed. At study completion, the senior author examined the data for extreme or missing values and inconsistencies in static variables (ie, gender) for patients with multiple hospitalizations.

Analyses

The cohort was described with summary statistics. Univariate mixed regression models were used to test for association between the predictors and primary and secondary outcome variables. Variables that were statistically significant in the univariate regression analyses were subsequently evaluated in a multivariate mixed model (logistic for admission; linear for all secondary outcome variables). The final multivariate model was determined by using backward stepwise variable selection in addition to clinical consideration. The mixed models included patient random effects to account for multiple ED visits from certain subjects. Missing data were excluded from the analysis. All analyses were performed by using SAS 9.2 (SAS Institute, Cary, NC).

RESULTS

Descriptive Characteristics of Cohort

SCD patients made 2864 ED visits within the 3-year study frame. After ineligible visits were excluded, the final cohort consisted of 414 visits from 177 patients (Fig 1). The median number of ED visits was 2 (range 1–18). The median age for patients was 13.4 years, and 47% were female (Table 1). The majority of patients had hemoglobin SS disease (sickle cell anemia, 63%) and health insurance coverage by Medicaid (67%). No data were missing for the primary outcome or predictor variables. Three patients were missing the secondary outcomes of pain score AUC and change in pain scores 1 and 2. The covariates missing data were hemoglobin (n = 3) and reticulocytes (n = 7) in the ED.

ED Times

Beginning with patient registration, the process of opioid administration was widely variable in duration and included a rapid triage (median duration 2.5 minutes) and rooming process (median duration 12 minutes) (Table 1). After patients were given rooms, the median duration to opioid order entry by a provider was 42 minutes. Opioid administration occurred at a median of 30 minutes after order entry. The median total TTO from registration was 86 minutes (range 10–405). The median total time in the ED was 390 minutes (range 80–1545).

Admission

Inpatient admission occurred in 53% (n = 219) of ED visits for VOC. The median TTO for admitted patients was 86 minutes vs 87 minutes for those not admitted. In univariate regression, TTO was not associated with admission (TTO quartile 1 [≤55 minutes] versus quartile 4 [≥131 minutes, referent], odds ratio 1.46, 95% confidence interval [CI] 0.82 to 2.59). In the multivariate analysis, the only predictor variables associated with increasing likelihood of admission were older age, larger number of VOC admissions for the previous year, and pain location in the chest (Table 2).

Change in First 2 Pain Scores

The mean improvement in the first 2 pain scores was 0.65 (5-point scale, SD 1.47). Three subjects had

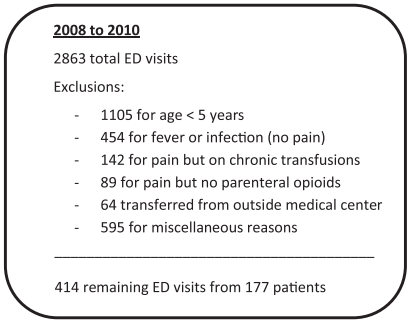

FIGURE 1
Reasons for exclusion of the 2863 ED visits initially identified from 2008 through 2010.

TABLE 1 Descriptive Characteristics of Cohort

Patient (n = 177) and Visit (n = 414) Attributes	Result
Age, y	13.4 (9.3–16.5)
Gender	
Male	53.7
Female	46.3
Sickle genotype	
SS	62.7
SC	26.0
Sβ^0	1.7
Sβ^+	9.6
Inpatient admissions in preceding 12 mo	
0	58.2
1	23.9
≥2	17.9
Primary payer	
Medicaid	67.2
Private insurance	30.9
Other	1.9
Pain location (not mutually exclusive)	
Chest	22.7
Left leg	40.8
Right leg	44.0
Left arm	20.1
Right arm	20.8
Back	29.0
Abdomen	10.6
Other, including "all over"	5.1
Arrival by ambulance	4.8
Temperature at triage, °C	37.0 (36.6–37.3)
Hemoglobin in ED, g/dL	8.7 (7.7–10.2)
Hemoglobin at baseline, g/dL	8.8 (7.7–10.1)
First intravenous opioid	
Morphine	96.9
Hydromorphone	1.9
Other	1.2
Dose of first intravenous opioid, mg/kg morphine equivalent	0.095 (0.075–0.100)
First oral medication, n = 398 visits	
Ibuprofen	47.5
Acetaminophen with codeine	10.8
Acetaminophen with hydrocodone	39.7
Other	2
ED time intervals, min	
Registration to triage	2.5 (1–52)
Registration to room	14 (3–221)
Registration to opioid order by provider	56 (8–298)
Registration to opioid administration, TTO	86 (10–405)
Total ED length of stay, registration to discharge or transfer	390 (80–1545)

Data are presented as the median (IQR) or %. Sβ^0, sickle β^0 thalassemia; Sβ^+, sickle β^+ thalassemia; SC, sickle hemoglobin C disease; SS, sickle cell anemia.

a first pain score without a second documented pain score and were excluded from the analysis. The median duration between the first 2 pain scores was 61 minutes. In univariate regression, decreased TTO was associated with greater improvements between the first 2 pain scores (TTO quartile 1 [≤55 minutes] versus quartile 4 [≥131 minutes, referent], β coefficient 0.77, 95% CI 0.33 to 1.21). In multivariate analysis, decreased TTO was again associated with greater improvements in pain scores 1 and 2, as were older age and higher first pain score (Table 3). These findings remained after adjusting for admission status.

Pain Score AUC

The median pain score AUC was 795 (interquartile range [IQR] 559–967). In univariate regression, decreased TTO was associated with decreased pain score AUC (TTO quartile 1 [≤55 minutes] versus quartile 4 [≥131 minutes, referent], β coefficient −87.0, 95% CI −161.0 to −13.0). In multivariate analysis, decreased TTO was again associated with decreased pain score AUC, as were lower age and lower first pain score (Table 3). The findings remained after adjusting for admission status.

Total ED Length of Stay

The median total ED length of stay was 390 minutes (IQR 302–525). In univariate regression, decreased TTO was associated with decreased total ED length of stay (TTO quartile 1 [≤55 minutes] versus quartile 4 [≥131 minutes, referent], β coefficient −121.2, 95% CI −181.6 to −60.7). In multivariate analysis, decreased TTO was again associated decreased total ED length of stay, as were discharge from the ED (as opposed to inpatient admission), decreased interval between pain scores 1 and 2, and presentation after EMR implementation (Table 4).

Total Dose of Parenteral Opioid

The median total dose of parenteral opioid was 0.18 mg/kg morphine equivalents (IQR 0.10–0.29). In univariate regression, decreased TTO was associated with increased total dose of parenteral opioid (TTO quartile 1 [≤55 minutes] versus quartile 4 [≥131 minutes, referent], β coefficient 0.042, 95% CI 0.009 to 0.076). In multivariate analysis, decreased TTO was again associated with an increased total dose of parenteral opioids, as were larger number of VOC admissions for the previous year, larger number of pain locations, and admission status (Table 4).

DISCUSSION

In a pediatric SCD population with VOC, we observed wide variability in the time between arrival and

TABLE 2 Multivariate Model of Primary Outcome: Admission Status

Predictor Variable	Admitted, %	Odds Ratio	95% CI
VOC admission in previous 12 mo			
0	44.4	Referent	
1	62.6	1.98	1.22–3.23
≥2	66.2	2.02	1.10–3.72
Pain location			
Other locations	49.1	Referent	
Chest	64.9	1.72	1.04–2.86
Age quartiles, mo			
≤102	36.7	Referent	
103–144	50.7	2.00	1.12–3.54
145–186	56.6	2.17	1.19–3.96
>186	60.8	2.41	1.40–4.17

The primary predictor, TTO, was not associated with admission status in univariate or multivariate modeling.

administration of standard treatment, intravenous opioids. Decreased TTO was not associated with admission but was associated with greater improvements in the first 2 pain scores, improved total pain over the first 4 hours of an ED visit, and decreased total ED length of stay. TTO was also associated with the receipt of increased total intravenous opioids, which may be attributable to the observation that those in the lowest quartile of TTO had the highest initial pain scores.

TABLE 3 Multivariate Models of Secondary Outcomes: Change in Pain Scores 1 and 2 and Pain Score AUC

Predictor Variable	Parameter Estimate, mean (SE)	β Coefficient	95% CI
Change in pain scores 1 and 2, 5-point pain score			
TTO (min)			
1st quartile (≤55)	1.07 (0.18)	.53	.12 to .95
2nd quartile (56–87)	0.88 (0.14)	.49	.17 to .80
3rd quartile (88–130)	0.36 (0.14)	.11	−.18 to .40
4th quartile (≥131)	0.29 (0.10)	Referent	
Age quartile, mo			
≤102	0.50 (0.10)	Referent	
103–144	0.64 (0.13)	.09	−.22 to .41
145–186	0.31 (0.17)	−.17	−.58 to .25
>186	1.21 (0.20)	.81	.39 to 1.22
First pain score			
≤3	−0.27 (0.20)	Referent	
4	0.45 (0.11)	.72	.28 to 1.18
5	1.05 (0.09)	1.27	.81 to 1.74
Pain score AUC (maximum = 1200, 240 min × pain score 5)			
TTO (min)			
1st quartile (≤55)	716 (29)	−171	−239 to −102
2nd quartile (56–87)	724 (29)	−132	−200 to −63
3rd quartile (88–130)	759 (28)	−68	−127 to −10
4th quartile (≥131)	840 (29)	Referent	
Age quartile, mo			
≤102	557 (33)	Referent	
103–144	797 (31)	214	130 to 298
145–186	796 (26)	165	91 to 240
>186	838 (21)	214	138 to 290
Admission status			
Admitted	859 (17)	160	109 to 210
Discharged from ED	645 (21)	Referent	
First pain score			
≤3	550 (33)	Referent	
4	745 (24)	180	119 to 241
5	832 (19)	268	211 to 325

TTO has been described in SCD populations in previous studies, but whether it is associated with outcomes has not been addressed. One previous study has described TTO in adult SCD patients and found a similar median of 90 minutes.[7] In that study, predictors of prolonged TTO included lower triage priority level and female gender. Previous reports have also examined disparities in time to treatment in the ED for SCD patients compared with other painful conditions. Interestingly, discrepant observations were made between adults and children. In pediatric patients, a recent case-control study of 152 cases of VOC demonstrated no differences in TTO (defined as time from first pain score in triage to administration of first analgesia) compared with race-matched patients with long-bone fracture.[21] In that study, the mean TTO was 68 minutes, which is comparable to our observations. By contrast, a retrospective cohort study comparing adults with VOC to those with renal colic found a mean TTO of 80 minutes for SCD compared with 50 minutes for renal colic.[22] Additionally, a cross-sectional analysis of the National Hospital Ambulatory Medical Care Survey found that adult SCD patients (mean age 27.6 years) with VOC experienced longer wait times to see a physician compared with both the general population and patients with long-bone fracture, although TTO was not compared between groups.[23] Treatment delays for VOC may be deleterious due to underlying pain biology. When noxious stimuli are presented to peripheral sensory neurons, expression of c-fos is increased in neurons in the dorsal horn of the spinal cord, which can lead to enhanced pain responses to subsequent or ongoing stimuli.[24] Hence, delays in provision of analgesia may worsen a VOC episode.[7] The likelihood of the development of chronic pain may increase as a result.

Two prevailing theoretical frameworks for QOC include Donabedian's model of structure-

TABLE 4 Multivariate Models of Secondary Outcomes: Total ED Length of Stay and Total Opioid Dose in the ED

Predictor Variable	Parameter Estimate, Mean (SE)	β Coefficient	95% CI
Total ED length of stay, min			
TTO (min)			
1st quartile (≤55)	406 (21)	−123	−184 to −63
2nd quartile (56–87)	400 (20)	−111	−161 to −60
3rd quartile (88–130)	442 (23)	−82	−135 to −30
4th quartile (≥131)	531 (22)	Referent	
Admission status			
Inpatient admission	520 (17)	160	120 to 200
Discharge from the ED	360 (11)	Referent	
Interval between pain scores 1 and 2	Not applicable	.52	.11 to .94
Before or after EMR installation			
Before EMR	480 (18)	61	23 to 98
After EMR	412 (13)	Referent	
Total opioid dose in ED, mg/kg morphine equivalent			
TTO (min)			
1st quartile (≤55)	0.22 (0.01)	.034	.007 to .062
2nd quartile (56–87)	0.20 (0.01)	.019	−.006 to .043
3rd quartile (88–130)	0.19 (0.01)	.008	−.022 to .039
4th quartile (≥131)	0.19 (0.01)	Referent	
Admission status			
Inpatient admission	0.27 (0.01)	.131	.110 to .153
Discharged from the ED	0.13 (0.01)	Referent	
Number of pain locations			
1	0.18 (0.01)	Referent	
2	0.20 (0.01)	.010	−.012 to .031
3	0.24 (0.02)	.031	.002 to .059
4	0.25 (0.03)	.065	.013 to .117
VOC admission in previous 12 mo			
0	0.18 (0.01)	Referent	
1	0.23 (0.01)	.013	.003 to .053
≥2	0.24 (0.02)	.017	−.001 to .067

process-outcome[25] and the Institute of Medicine's 6 domains of quality including safety, effectiveness, timeliness, patient-centeredness, efficiency, and equitability.[26] TTO is classified as a process measure in the Donabedian model and reflects the timeliness, patient-centeredness, and efficiency domains from the Institute of Medicine model. The appeal of many broadly applied process measures (such as the time to intervention in sepsis) is the association of process with outcomes. To that end, this study sought to broaden the obvious appeal of TTO by identifying associations of TTO with outcomes of care for VOC patients in the ED. Although TTO was not associated with this study's primary outcome (hospital admission), the association of TTO with our secondary outcomes bolsters its validity as a process measure. In addition, TTO's association with outcomes of ED visits suggests that TTO reflects the effectiveness of care for VOC in addition to the previously mentioned domains of QOC.

The predictors for VOC admission identified in this study (increased number of previous admissions, increasing age, and pain location in the chest) have not been previously reported. It has been reported that VOCs become more numerous and more intense as children age, so the finding of increasing age is not surprising.[8] Similarly, a history of frequent VOCs is associated with subsequent VOCs, which likely explains the finding of increased admissions in the past 12 months in association with admission.[27] In addition, chest pain may increase the risk for admission due to the concern for impending acute chest syndrome. In 1995, Frusch et al[28] examined children with SCD presenting to the Duke University pediatric ED to identify predictors of admission. They found that a shorter duration of pain before presentation in afebrile patients was associated with increased likelihood of admission and that there was no correlation between pain location and admission.[28] In this retrospective study, we were unable to reliably assess the duration of pain and, therefore, cannot evaluate its importance relative to our identified predictors.

Implementation of an EMR has been associated with variable impacts on the timeliness of care in previous studies.[29,30] Frequently, the timeliness of care is transiently increased before returning to pre-implementation levels.[31] In this study, we found an independent association of post-EMR implementation with decreased total ED length of stay. Implementation of the EMR was concomitant with ongoing efforts in our ED to improve throughput and decrease total length of stay, which may serve as a confounder to EMR implementation and may better explain the observation of decreased length of stay.

Our study is limited by the single-center design and the inherent imperfections in the medical record, including potential inaccurate recordings. In addition, retrospective cohorts are prone to selection bias. To circumvent this problem, our subject identification intentionally lacked specificity for VOC and included all ED visits for SCD patients. Another limitation is the potential for error in retrospectively identifying patients with VOC, which is a clinically defined syndrome and involves the subjective patient experience of pain. Additionally, our study frame spanned the introduction of an EMR. We observed that charted times throughout the record were more

precise with electronic charting. Although pain scores are inherently subjective as measures of pain intensity, they are the best method currently available. Another potential limitation is the overrepresentation of a small subset of clinically severe patients in the data set. Our statistical modeling approach attempts to mitigate this problem but is imperfect.

CONCLUSIONS

TTO is independently associated with important outcomes of ED visits for children with SCD, including improved pain scores, shorter length of stay, and increased opioid delivery. Due to the severe nature of the pain in VOC, efforts to reduce TTO are of paramount importance. To that end, we now track TTO in our center and are planning a quality improvement initiative to aid in early identification of patients with VOC to achieve a goal TTO of <60 minutes. In addition, research is needed to (1) evaluate TTO in other populations, (2) further assess reasons for prolonged TTO, and (3) identify effective practices to reduce TTO. Finally, we propose that TTO should be included in the quality "dashboard" for both EDs and day hospitals involved in urgent care for children with SCD.

ACKNOWLEDGMENTS

The authors thank Dr George R. Buchanan for his thoughtful review of the manuscript, Dr Song Zhang for his review of the statistical plan and analyses, and Ms Hailey Hodgkiss for her help in data collection.

REFERENCES

1. Ballas SK, Lieff S, Benjamin LJ, et al; Investigators, Comprehensive Sickle Cell Centers. Definitions of the phenotypic manifestations of sickle cell disease. *Am J Hematol*. 2010;85(1):6–13
2. Hassell KL. Population estimates of sickle cell disease in the U.S. *Am J Prev Med*. 2010;38(4 suppl):S512–S521
3. Steiner C, Miller J. *Sickle Cell Disease Patients in U.S. Hospitals, 2004: Statistical Brief* #21. Healthcare Cost and Utilization Project, Rockville, MD. Agency for Healthcare Policy and Research; 2006:1–9
4. Brandow AM, Brousseau DC, Panepinto JA. Postdischarge pain, functional limitations and impact on caregivers of children with sickle cell disease treated for painful events. *Br J Haematol*. 2009; 144(5):782–788
5. Frei-Jones MJ, Baxter AL, Rogers ZR, Buchanan GR. Vaso-occlusive episodes in older children with sickle cell disease: emergency department management and pain assessment. *J Pediatr*. 2008; 152(2):281–285
6. Solomon LR. Treatment and prevention of pain due to vaso-occlusive crises in adults with sickle cell disease: an educational void. *Blood*. 2008;111(3): 997–1003
7. Tanabe P, Myers R, Zosel A, et al. Emergency department management of acute pain episodes in sickle cell disease. *Acad Emerg Med*. 2007;14(5):419–425
8. Platt OS, Thorington BD, Brambilla DJ, et al. Pain in sickle cell disease. Rates and risk factors. *N Engl J Med*. 1991; 325(1):11–16
9. Orringer EP, Casella JF, Ataga KI, et al. Purified poloxamer 188 for treatment of acute vaso-occlusive crisis of sickle cell disease: a randomized controlled trial. *JAMA*. 2001;286(17):2099–2106
10. Gladwin MT, Kato GJ, Weiner D, et al; DeNOVO Investigators. Nitric oxide for inhalation in the acute treatment of sickle cell pain crisis: a randomized controlled trial. *JAMA*. 2011;305(9):893–902
11. Benjamin LJ, Swinson GI, Nagel RL. Sickle cell anemia day hospital: an approach for the management of uncomplicated painful crises. *Blood*. 2000;95(4):1130–1136
12. Tanabe P, Dias N, Gorman L. Care of children with sickle cell disease in the emergency department: parent and provider perspectives inform quality improvement efforts. *J Pediatr Oncol Nurs*. 2013;30(4):205–217
13. Glassberg JA, Tanabe P, Chow A, et al. Emergency provider analgesic practices and attitudes toward patients with sickle cell disease. *Ann Emerg Med*. 2013;62(4): 293–302.e210
14. Murray N, May A. Painful crises in sickle cell disease—patients' perspectives. *BMJ*. 1988;297(6646):452–454
15. Maxwell K, Streetly A, Bevan D. Experiences of hospital care and treatment seeking for pain from sickle cell disease: qualitative study. *BMJ*. 1999; 318(7198):1585–1590
16. Wang CJ, Kavanagh PL, Little AA, Holliman JB, Sprinz PG. Quality-of-care indicators for children with sickle cell disease. *Pediatrics*. 2011;128(3):484–493
17. Alessandrini E, Varadarajan K, Alpern ER, et al; Pediatric Emergency Care Applied Research Network. Emergency department quality: an analysis of existing pediatric measures. *Acad Emerg Med*. 2011;18(5):519–526
18. Smith JE, Rockett M, Squire R, et al. PAin SoluTions In the Emergency Setting (PASTIES); a protocol for two open-label randomised trials of patient-controlled analgesia (PCA) versus routine care in the emergency department. *BMJ Open*. 2013;3(2):e002577
19. Gordon DB, Stevenson KK, Griffie J, Muchka S, Rapp C, Ford-Roberts K. Opioid equianalgesic calculations. *J Palliat Med*. 1999;2(2):209–218
20. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap)—a metadata-driven methodology and workflow process for providing translational research informatics support. *J Biomed Inform*. 2009;42(2):377–381
21. Zempsky WT, Loiselle KA, McKay K, Lee BH, Hagstrom JN, Schechter NL. Do children with sickle cell disease receive disparate care for pain in the emergency department? *J Emerg Med*. 2010;39(5):691–695
22. Lazio MP, Costello HH, Courtney DM, et al. A comparison of analgesic management for emergency department patients with sickle cell disease and renal colic. *Clin J Pain*. 2010;26(3):199–205
23. Haywood C Jr, Tanabe P, Naik R, Beach MC, Lanzkron S. The impact of race and disease on sickle cell patient wait times in the emergency department. *Am J Emerg Med*. 2013;31(4):651–656
24. Coggeshall RE. Fos, nociception and the dorsal horn. *Prog Neurobiol*. 2005;77(5): 299–352
25. Donabedian A. The quality of care. How can it be assessed? *JAMA*. 1988;260(12):1743–1748

26. Institute of Medicine (U.S.); Committee on Quality of Health Care in America. Crossing the Quality Chasm: a New Health System for the 21st Century. Washington, D.C.: National Academy Press; 2001
27. Quinn CT, Shull EP, Ahmad N, Lee NJ, Rogers ZR, Buchanan GR. Prognostic significance of early vaso-occlusive complications in children with sickle cell anemia. *Blood*. 2007;109(1):40–45
28. Frush K, Ware RE, Kinney TR. Emergency department visits by children with sickle hemoglobinopathies: factors associated with hospital admission. *Pediatr Emerg Care*. 1995;11(1):9–12
29. Ward MJ, Landman AB, Case K, Berthelot J, Pilgrim RL, Pines JM. The effect of electronic health record implementation on community emergency department operational measures of performance. *Ann Emerg Med*. 2014;63(6):723–730
30. Connelly DP, Park YT, Du J, et al. The impact of electronic health records on care of heart failure patients in the emergency room. *J Am Med Inform Assoc*. 2012;19(3):334–340
31. Spellman Kennebeck S, Timm N, Farrell MK, Spooner SA. Impact of electronic health record implementation on patient flow metrics in a pediatric emergency department. *J Am Med Inform Assoc*. 2012;19(3):443–447

MEN'S WALLETS: *During the past few weeks I have been flooded with advertisements for men's fashion accessories. I will occasionally peruse the wallets, but never with too much interest. Although I am in my sixth decade, I have only owned three wallets in my life and do not anticipate purchasing another any time soon. As reported in* The Wall Street Journal *(Fashion: December 12, 2014), buying a wallet is almost like a rite of passage for men. Most wallets are made of nylon or leather and have compartments for bills, cards, and oftentimes coins. Recently, as with many other men's fashion accessories, there has been an explosion in the variety of offerings. Wallets come in an array of leathers, fabrics, stitching, and embroidery. A wallet may seem a relatively safe holiday present, but given that men may use the wallet for a long time or use them as a fashion statement, considerable thought should go into the purchase. Sellers of wallets usually suggest getting to know the person and what he likes to carry before making the purchase. The first wallet I purchased was made of cow hide leather similar to the one my father carried. One of my sons took a very different route, crafting his first wallet from duct tape. Another son uses the much worn and somewhat tattered second wallet I ever owned. Evidently, wallets range in price from a few dollars to more than $2000. While gorgeous, I certainly do not need a dyed crocodile leather wallet.*

A few years ago, my wife, noticing the grave state of my wallet at the time, gave me a gorgeous slim billfold made from water buffalo hide in a popular style. I like the thinness and the fact that the leather softens and colors with age. I think it should last a very long time and may be the last wallet I ever own.

Noted by WVR, MD

Timing of Opioid Administration as a Quality Indicator for Pain Crises in Sickle Cell Disease

Melissa D. Mathias and Timothy L. McCavit

Pediatrics 2015;135;475
DOI: 10.1542/peds.2014-2874 originally published online February 9, 2015;

PEDIATRICS®
OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF PEDIATRICS

Timing of Opioid Administration as a Quality Indicator for Pain Crises in Sickle Cell Disease

Melissa D. Mathias and Timothy L. McCavit

Pediatrics 2015;135;475
DOI: 10.1542/peds.2014-2874 originally published online February 9, 2015;