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Abstract

Transcranial Doppler (TCD) screening rates remain low among children with sickle cell disease (SCD). We assessed TCD screening rates and missed opportunities for TCD screening. Children 2 to 16 years old with SCD enrolled in Michigan Medicaid for ≥1 year (2007-2011) were identified through newborn screening. Receipt of TCD screening and presence of a missed opportunity (≥1 SCD-related outpatient visit, no TCD screening) were identified through administrative claims. Potential correlates of missed opportunities included SCD-related health services, comorbidities, and demographics. Logistic regression with generalized estimating equations modeled associations between a missed opportunity and correlates. Overall, 353 children contributed 1066 person-years. TCD screening was low yearly (10%-32%); missed opportunities occurred in 73% of the person-years. Increasing age (odds ratio [OR] = 1.11; confidence interval CI = 1.07, 1.15), previous TCD screening (OR = 0.26; CI = 0.16, 0.41), and 4 to 5 (OR = 0.48; CI = 0.26, 0.87) or ≥6 outpatient visits (OR = 0.26; CI = 0.14, 0.49) were associated with a missed opportunity. Reduction of missed opportunities is a potential strategy to increase TCD screening rates.

Keywords

sickle cell disease, pediatric stroke, stroke prevention, transcranial Doppler screening, health services research, children, Medicaid, newborn screening

Introduction

Children with sickle cell disease (SCD) are at an increased risk for stroke.[1-3] Without intervention, 11% of children with SCD are expected to have a stroke by the age of 20 years; however, the majority of these strokes are now considered preventable.[4-6] Transcranial Doppler (TCD) screening detects blood velocities in cerebral vessels; high velocities are indicative of a high stroke risk and indicate the need to begin preventive efforts in the form of blood transfusions to maintain low hemoglobin (Hb) concentrations.[7]

The Stroke Prevention in Sickle Cell Anemia (STOP) trial in 1998 found that stroke risk was reduced by 92% in children receiving chronic blood transfusions after detection of high blood velocities by TCD screening as compared with those not receiving transfusions.[8] The National Heart, Lung and Blood Institute (NHLBI) released guidelines in 2002 recommending that TCD screening be initiated for children with SCD at 2 years old, and if TCD results show normal blood velocities, children are recommended to subsequently receive 1 screening annually until 16 years old.[9] This recommendation was further emphasized in 2014 with newly released NHLBI guidelines, which continue to strongly recommend TCD screening among children with SCD.[10]

Health care use is often high in children with SCD because this population has 7 to 30 times the hospitalization rates, 2 to 6 times the emergency department (ED) visits, and more than 8 times the health care expenditures

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compared with their counterparts without SCD.[11-14] Even with frequent contact with the health care system, TCD screening rates are still substantially lower than that recommended by the NHLBI guidelines.[15,16] One contributing factor may be missed opportunities for TCD screening, where a child with SCD who is eligible for screening has a health service encounter, yet does not have a TCD screen performed. This missed opportunity framework has been utilized successfully in the immunization literature to identify interventions to increase immunization rates.[17,18] To our knowledge, missed opportunities have never been explored in relation to TCD screening in children with SCD; however, we hypothesized that missed opportunities for TCD screening may be numerous in children with SCD and provide an appropriate intervention target, given the frequent health care interactions and low TCD screening rates among children with SCD. Therefore, the objectives of this study were to (1) assess TCD screening rates, (2) calculate the frequency and predictors of missed opportunities for TCD screening in children with SCD enrolled in Michigan Medicaid, and (3) estimate the maximum TCD screening rates potentially achievable through reductions in missed opportunities based on these findings.

Methods

Data Sources

Administrative data from Michigan Medicaid for the years 2007 to 2011 were queried from the Michigan Department of Health and Human Services (MDHHS) data warehouse, including enrollment history and claims for inpatient, ED, outpatient, and pharmacy services. Michigan Medicaid enrollees were linked to newborn screening results through birth certificates to identify children with SCD born from 1987 to 2008, and all administrative claims were obtained for children with SCD.[19]

Study Population

Children 2 to 16 years of age with SCD were identified as those having HbSS or HbS/βthalassemia.[8-10] Children were eligible for the study if they were continuously enrolled in Michigan Medicaid with no other forms of health insurance for at least 1 calendar year (January 1 to December 31) from 2007 to 2011; a 1-month gap in enrollment was allowed each year. Children with receipt of 6 or more blood transfusions in a year were excluded because transfusions may be indicative of prior stroke or high blood velocities as detected by previous TCD.[7,8] Blood transfusions were identified through CPT codes of 09882, 09883, 36430, 36455, 86999, S3906, or S9538 on any claim. Children with unknown date of birth were also excluded.

Receipt of TCD Screening and Presence of Missed Opportunities for TCD Screening

Two outcomes were identified for each year the child was in the study population: (1) receipt of at least 1 TCD screening and (2) presence of a missed opportunity for TCD screening. Receipt of TCD screening was defined as having any claim with a CPT code of 93886, 93888, 93890, 93892 or 93893.[20] A missed opportunity was defined as having an SCD-related outpatient visit with no receipt of TCD screening within the same year.[21] Consistent with other studies, we included diagnosis codes in any position for sickle cell anemia (282.60, 282.61, and 282.62) and HbS/βthalassemia (282.41 and 282.42) as well as HbSC (282.63 and 282.64) and HbSD (282.68 and 282.69).[22-24]

Correlates of Missed Opportunities

Identification of correlates of missed opportunities may detect specific subgroups of children that could be targeted to reduce missed opportunities. We identified a subset of children within our study population who were enrolled for at least 2 consecutive years in Michigan Medicaid from 2007 to 2011 (children could contribute multiple time intervals). Two consecutive years of enrollment was required to ensure that the potential correlates occurred prior to the missed opportunity (ie, to preserve the temporal relationship). We investigated the following correlates: SCD-related health care encounters (ED, inpatient, outpatient, and hematologist visits), SCD comorbidities (pneumococcal infection and severity of disease),[15] previous receipt of TCD screening, sickle cell subtype (HbSS, HbS/βthalassemia), and demographics (age, sex). With the exception of age, all correlates were characterized in the first year of continuous enrollment, and the presence of a missed opportunity was assessed in the following year (year 2 of continuous enrollment). Children with no SCD-related outpatient visits in year 2 were excluded from this analysis.

Pneumococcal infection was identified as any nonpreventive health care claim with an ICD-9 code of 038.0, 038.2, 481, 482.3, 482.9, or 486.[25] A proxy for severity of disease was determined using the number of inpatient visits per year with children: 2 or more inpatient visits was considered indicative of severe SCD.[15] ED, inpatient, and outpatient (both preventive and nonpreventive) visits were identified using the ICD-9 CM codes for SCD. Hematologist visits were defined as having at least 1 visit in Medicaid claims with a hematologist identified through (1) pediatric hematologists from the American Medical Association (AMA) Masterfile or (2) an Internet search of pediatric hematologists; subsequently, all hematologists were verified as a board-certified

Table 1. Baseline Demographics of Children With Sickle Cell Disease Enrolled in Michigan Medicaid in 2007, n = 231.

	n (%) or Mean (SD)
Gender	
Male	115 (50)
Female	116 (50)
Race	
Black	222 (96)
White	2 (1)
Unknown	7 (3)
Sickle cell subtype	
Hemoglobin SS	201 (87)
Hemoglobin S/βthalassemia	30 (13)
Age on January 1, 2007 (years)	10.5 (4.1)

hematologist using the National Provider Index (NPI). Previous receipt of TCD screening was identified through CPT codes for TCD as described above and also measured in year 1 of continuous enrollment. Age and sex were from Medicaid eligibility files; age was determined as the child's age on January 1 of the second year of continuous enrollment. Sickle cell type was defined as either HbSS or HbS/βthalassemia as obtained from newborn screening records.

Statistical Analysis

Frequencies and percentages or means and standard deviations (SDs) were determined for all demographics. The proportion of children receiving TCD screening was calculated annually (2007-2011) and by age groups of 2 to 6 years, 7 to 11 years, and 12 to 16 years. The proportion of missed opportunities was calculated annually and for the overall study period. The maximum potentially achievable TCD screening rate was estimated for 25%, 50%, 75%, and 100% reductions in missed opportunities based on TCD screening rates and missed opportunities in 2011.

Frequencies and percentages or means and SDs were calculated for potential correlates of a missed opportunity. Logistic regression with generalized estimating equations (GEEs) was used to estimate the association between each correlate and the presence of at least one missed opportunity. GEE models with robust standard errors were estimated to account for the correlation within children because each child could contribute multiple 2-year time intervals.[26] Alternative functional forms for continuous variables were investigated; based on the Quasi-Akaike Information Criterion for each model, we determined that SCD-related inpatient visits, ED visits, and age should be modeled as continuous variables, whereas SCD-related outpatient visits was modeled using indicator variables based on quintiles (1 visit, 2 visits, 3 visits, 4-5 visits, and 6+ visits).[26] Hematologist visits and pneumococcal infection were included as dichotomous variables, in addition to sickle cell subtype (HbSS vs HbS/βthalassemia), sex (male vs female), severity of disease, and previous receipt of TCD screening. Covariates showing an association ($P < .20$) with a missed opportunity were included in a final multivariable model.

The study was approved by the institutional review board of the University of Michigan (#HUM00051878).

Results

A total of 638 children with HbSS or HbS/βthalassemia born between 1987 and 2008 were identified in Michigan Medicaid claims from 2007 to 2011. Among these children, 40 (6.2%) were missing date-of-birth information. An additional 124 children (19.4%) were not continuously enrolled for at least 1 year, for a total of 474 children contributing 1831 person-years of enrollment. From 2007 to 2011, 179 person-years were excluded because of receipt of at least 6 transfusions, and 586 person-years did not meet the age requirement of 2 to 16 years. The final study population consisted of 353 unique children contributing 1066 person-years. Among the 353 eligible children, 85 contributed 1 year of enrollment (24%), 67 contributed 2 years (19%), 56 contributed 3 years (16%), 46 contributed 4 years (13%), and 99 contributed 5 years of enrollment (28%). In 2007, among 231 eligible children, the average age was 10.5 years (SD = 4.1); 50% were female; and 87% were sickle cell subtype HbSS (Table 1).

TCD Screening and Missed Opportunities

Overall, 159 of 353 eligible children (45%) received screening at least once from 2007 to 2011. Receipt of TCD screening was low each year (10% to 32%), although the proportion of children receiving TCD screening did increase over the study period (Figure 1). Children 2 to 6 years old had the highest likelihood of screening (38%), and rates decreased with increasing age; 20% of children 7 to 11 years old and 14% of 12- to 16-year-olds received screening from 2007 to 2011.

A total of 196 person-years did not include a SCD-related outpatient visit and were excluded, resulting in 307 children contributing 870 person-years for quantification of missed opportunities. The frequency of missed opportunities was high, ranging from 61% to 88% per year; 73% of all person-years contained a missed opportunity (Figure 2).

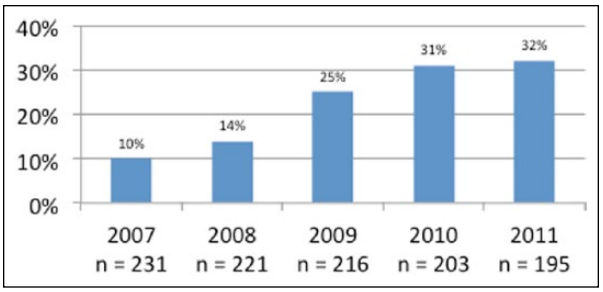

Figure 1. Receipt of transcranial Doppler screening among children with sickle cell disease enrolled in Michigan Medicaid for at least 1 year, 2007 to 2011.

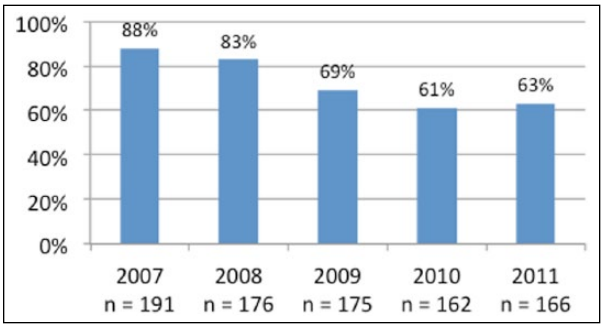

Figure 2. Frequency of missed opportunities in children enrolled in Michigan Medicaid for at least 1 year, from 2007 to 2011, with sickle cell disease and at least 1 sickle cell disease–related outpatient visit.

Increasing Screening Rates Through Reduction of Missed Opportunities

Based on 2011 rates (63% of children had a missed opportunity; 32% of children received TCD screening), a 25% reduction in missed opportunities would correspond to a 45% TCD screening rate among children with SCD. Similarly, a reduction in missed opportunities by 50% would lead to a TCD screening rate of 58% and by 75% to a screening rate of 72%; complete elimination of missed opportunities would lead to a screening rate of 85%.

Correlates of Missed Opportunities

A subset of 249 children (74%) was enrolled for at least 2 consecutive years and met eligibility criteria for analysis of potential correlates of missed opportunities. SCD-related health care encounters and presence of SCD comorbidities were relatively constant from 2007 to 2011; the majority had at least 1 hematologist visit in the first year of continuous enrollment; 12% to 20% had a pneumococcal infection; and 32% to 39% had at least 2 inpatient visits within a year (considered severe SCD; Table 2). Presence of a missed opportunity was associated with increasing age, previous receipt of TCD screening, SCD-related outpatient visits, SCD-related inpatient visits, presence of a pneumococcal infection, and at least 1 hematologist visit. In the multivariable logistic regression GEE model, a 1-year increase in age was associated with an increased likelihood of a missed opportunity (odds ratio [OR] = 1.11; confidence interval [CI] = 1.06, 1.15). Children with previous receipt of TCD screening (OR = 0.26; CI = 0.16, 0.41) were less likely to have a missed opportunity than those without a previous screening, along with children with 4 to 5 outpatient visits (OR = 0.48; CI = 0.26, 0.87) or 6 or more outpatient visits (OR = 0.26; CI = 0.14, 0.49) compared with children with 1 outpatient visit (Table 3).

Discussion

TCD screening rates were low among children with SCD in the Michigan Medicaid population, although rates increased over the study period. Low rates of screening combined with frequent interactions with the health care system led to a high frequency of missed opportunities for screening, particularly in older children. This study suggests that even small reductions in missed opportunities could increase TCD screening rates substantially.

TCD screening rates were low across all ages (10% to 32% from 2007 to 2011), with only 14% of children 12 to 16 years old receiving screening. Previous studies in sickle cell centers have demonstrated higher overall rates of TCD screening, although a study in a large, managed health care plan also showed a trend toward increased screening rates in younger compared with older children.[15,16,27] Our results may be a more accurate reflection of screening rates in all children with SCD because of inclusion of children up to the age of 16 years, consistent with NHLBI recommendations.[9,10] Several studies have used administrative claims or a recent comprehensive visit for SCD to identify their study populations, which biases toward those who seek care and thus may be more likely to receive screening. A strength of this study is identification of the study population using newborn screening records, which allows inclusion of children with no SCD-related health care encounters (12%-15% per year). This likely contributed to our lower rates as compared with those in other studies. However, our rates of TCD screening may still be an underestimation of the true rate of screening among children with SCD as a result of the inclusion criterion of continuous enrollment for at least 1 year in Medicaid because children with gaps in insurance coverage may be less likely to receive TCD screening.

High SCD-related health care use coupled with low rates of TCD screening led to a high frequency of missed opportunities for TCD screening. The increase in missed

Table 2. Health Care Encounters and Comorbidities of Children With Sickle Cell Disease (SCD) Enrolled in Michigan Medicaid for at Least 2 Years From 2007 to 2011 and With at Least 1 SCD-Related Outpatient Visit.[a]

	2007-2008, n = 159	2008-2009, n = 151	2009-2010, n = 145	2010-2011, n = 153
	Mean (Standard Deviation)			
SCD-related inpatient visits	1.3 (1.7)	1.4 (1.9)	1.4 (1.7)	1.4 (1.9)
SCD-related outpatient visits	3.9 (3.5)	4.1 (3.1)	4.3 (3.6)	4.5 (3.5)
SCD-related emergency department visits	0.7 (1.3)	0.6 (0.9)	0.8 (1.2)	1.0 (1.6)
	n (%)			
Pneumococcal infection	19 (12)	25 (17)	29 (20)	19 (12)
Hematologist visit	148 (93)	133 (88)	122 (84)	130 (85)
Severe SCD[b]	59 (37)	51 (34)	57 (39)	49 (32)

[a]Covariates measured in year 1 of the 2 years of continuous enrollment.
[b]At least 2 inpatient visits within a year.

Table 3. Multivariable Associations With Presence of a Missed Opportunity for TCD Screening in Michigan Medicaid, 2007-2011.

		Odds Ratio	Confidence Interval	*P* Value
SCD-related outpatient visits	1 Visit	Reference	Reference	
	2 Visits	1.06	0.49, 2.26	.89
	3 Visits	0.76	0.39, 1.48	.42
	4-5 Visits	0.48	0.26, 0.87	.02
	6+ Visits	0.26	0.14, 0.49	<.0001
Previous TCD screening	Yes	0.26	0.16, 0.41	<.0001
	No	Reference		
Age		1.11	1.07, 1.15	<.0001
Inpatient SCD visit		1.00	0.90, 1.12	.93
Pneumococcal infection	Yes	0.78	0.46, 1.32	.36
	No	Reference		
Hematologist visit	Yes	1.11	0.55, 2.27	.76
	No	Reference		

Abbreviations: SCD, sickle cell disease; TCD, transcranial Doppler.

opportunities in older children may be partly a result of variation across guidelines in the ages recommended for TCD screening. Whereas the NHLBI recommends screening from ages 2-16, the American Heart Association suggests that screening begin at 2 years with more frequent screening in younger patients, with no specific guidelines for teenagers, and the American Academy of Pediatrics advises discussion of TCD screening for 1- to 13-year-old children if available.[9,28,29,10] Our results demonstrating an association between prior receipt of TCD screening and a decreased odds of a missed opportunity also indicate that the same children may be receiving TCD screening each year. These children may have physicians who are consistently recommending TCD screening, or other factors, such as patient knowledge of TCD screening or clinic-specific recommendation practices, may be leading to more consistent screening.

We hypothesized that increased ED, inpatient, outpatient, and SCD visits and SCD comorbidities would be associated with fewer missed opportunities; however, no associations were found between these potential correlates and missed opportunities, apart from increased outpatient visits. This is similar to a recent study that showed that children with one or more outpatient visits are 2 to 3 times more likely to receive TCD screening than children without an outpatient visit; however, we did not show a reduction in the odds of a missed opportunity until at least 4 outpatient visits.[27] Children with a high frequency of health care use may potentially be a higher-risk group, which may positively influence their likelihood of screening.

Other unmeasured factors, such as physician and patient barriers, could be playing a role in missed opportunities apart from the factors investigated in this study. Lack of knowledge and/or awareness regarding TCD screening guidelines among physicians could be contributing to underrecommendation for TCD screening and, therefore, missed opportunities.[30,31] Patient barriers such as distance to a TCD screening facility and

appointment adherence could also play a role in receipt of TCD screening, regardless of physician recommendation.[15,16,32] Furthermore, caregivers of children with SCD have been shown to perceive the stroke risk for their child to be low and may not realize the importance of TCD screening.[33] Additional research is needed to explore provider and patient-level factors that may influence missed opportunities to identify the most viable intervention targets in this high-risk population.

Reducing missed opportunities may be an appropriate strategy to increase TCD screening rates. Although identification of missed opportunities in immunization studies has allowed targeted interventions to increase vaccination rates, receipt of TCD screening differs from the receipt of a vaccination.[17,18] Vaccinations can often occur at the same location and time as a doctor appointment, whereas TCD screening often occurs off-site and at an appointment different from the contact with the physician. Therefore, novel strategies to identify opportunities to reduce missed opportunities are necessary. Approaches such as offering screening at the same time as a clinic appointment have previously been shown to be successful and may be acutely needed, given the substantial proportion of children with a missed opportunity identified in this study.[34]

Limitations to this study exist. Medicaid claims data were used to identify covariates; therefore, errors in CPT or ICD-9 codes could lead to potential misclassification of variables. If the screening was performed but the child's insurance was not billed for the TCD screening, receipt of TCD screening would have been underreported. However, a recent study assessing the accuracy of administrative claims demonstrated high sensitivity of claims to identify TCD screening when compared with documentation in the medical record.[35] We were unable to identify reasons for the missed opportunity. For example, data were unavailable to indicate whether a physician took appropriate clinical action in recommending a TCD screen, but external circumstances did not allow for the child's screen to be completed. Although not all children with SCD are enrolled in Michigan Medicaid, 70% of children with SCD born between 1987 and 2008 had a Medicaid ID, indicating that these data do capture the majority of children with SCD in Michigan. Finally, there may be other children with SCD in Michigan not identified through Michigan's Newborn Screening program; however, through the use of Newborn Screening records, we can accurately report that each child included in the study population did have SCD.

In conclusion, the proportion of children receiving TCD screening each year is low, and missed opportunities are numerous in children with SCD in the Michigan Medicaid population. Increasing age is associated with having a missed opportunity, whereas 4 or more SCD-related outpatient visits and receipt of TCD screening in the year prior are protective against missed opportunities. Identification of novel interventions to reduce missed opportunities for TCD screening may be an integral strategy to increase adherence to TCD screening recommendations, thereby reducing the incidence of pediatric stroke in this high-risk population.

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Author Contributions

All authors assisted in the design of this study; SLR and LMC conducted the analyses; SLR drafted the initial manuscript; all authors critically reviewed and revised the manuscript.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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