The Impact of Hemoglobin Level on Risk of End-Organ Damage (EOD) among Patients with Sickle Cell Disease – A Large-Scale, Longitudinal Analysis

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Disclosures

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Anemia Affects Most Patients with SCD[1,2]

SCD is an inherited, multifaceted anemia that is associated with lifelong morbidity and early mortality.[2]

Low Hb levels have been correlated with EOD such as stroke, CKD, ESRD, and PH.[3]

This study sought to estimate the relationship between Hb and the risk of EOD based on large-scale, longitudinal analyses of recent data in the US

CKD, chronic kidney disease; EOD, end-organ damage; ESRD, end-stage renal disease; Hb, hemoglobin; PH, pulmonary hypertension; SCD, sickle cell disease.

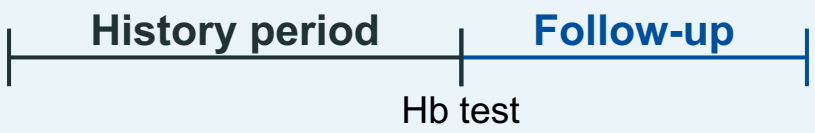
1. National Heart, Lung, and Blood Institute. Accessed November 5, 2020. https://www.nhlbi.nih.gov/health-topics/evidence-basedmanagement-sickle-cell-disease. 2. Kato GJ, et al. *Nat Rev Dis Primers.* 2018;4:18010. 3. Ataga KI, et al. *PLoS One*. 2020;15(4):e0229959.

Methods

- Patients with SCD aged ≥12 years and ≥1 Hb level reported from January 1, 2013 to July 31, 2020, in the large, US-representative, provider-centric Symphony Health claims database were included.
  - + Bivariate analyses of Hb levels and EOD were assessed using logistic GEE regression to account for clustering of observations at the patient level.
  - + Multivariable logistic GEE regression was employed to evaluate the independent association between Hb levels and EOD, adjusting for patient demographics and other SCD complications.

- For each patient, Hb values were identified and included as separate observations
- EOD occurring during the **follow-up period** and the **history period** were assessed

Prior and New EOD Evaluation



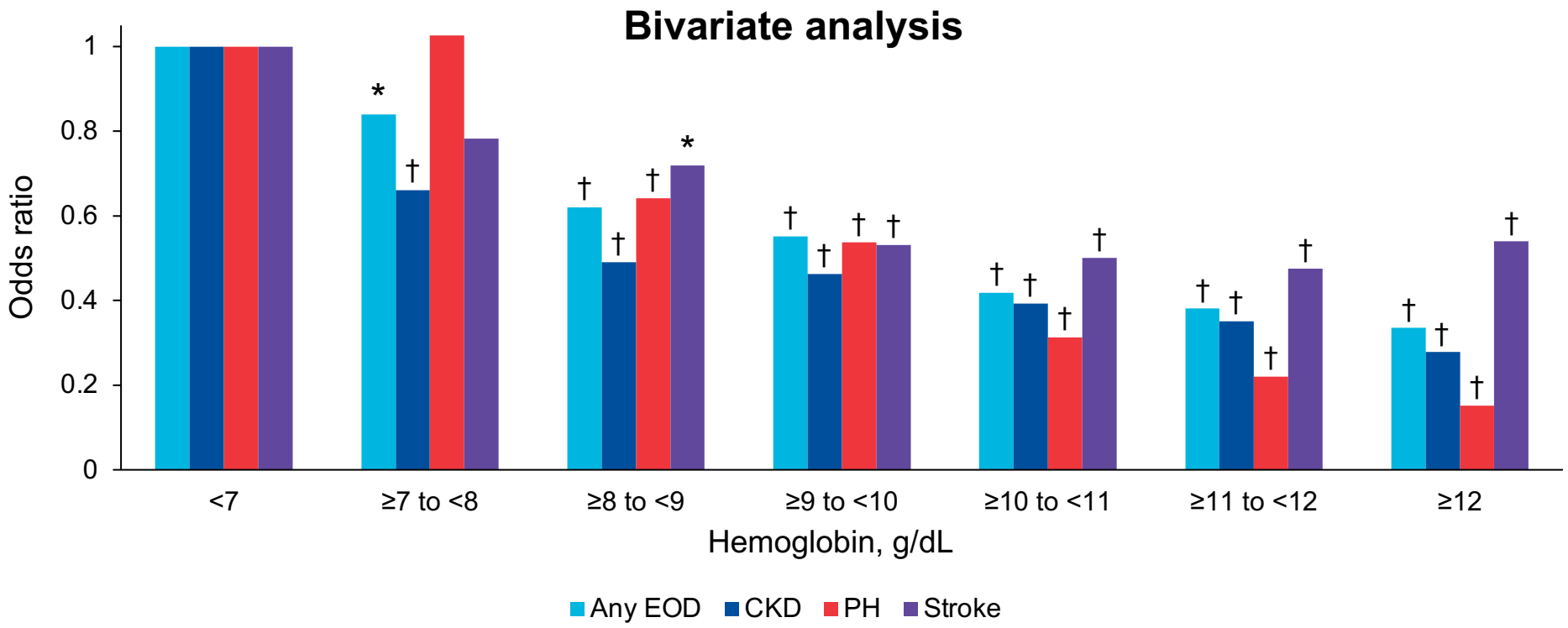
History period
(Jan 1, 2012 to Hb test dates)
- History of EOD and other comorbid conditions

Follow-up period (1-year post test)
- Onset of new EOD, including stroke, CKD, ESRD, and PH

CKD, chronic kidney disease; EOD, end-organ damage; ERSD, end-stage renal disease; GEE, generalized estimating equations; Hb, hemoglobin; PH, pulmonary hypertension; SCD, sickle cell disease.

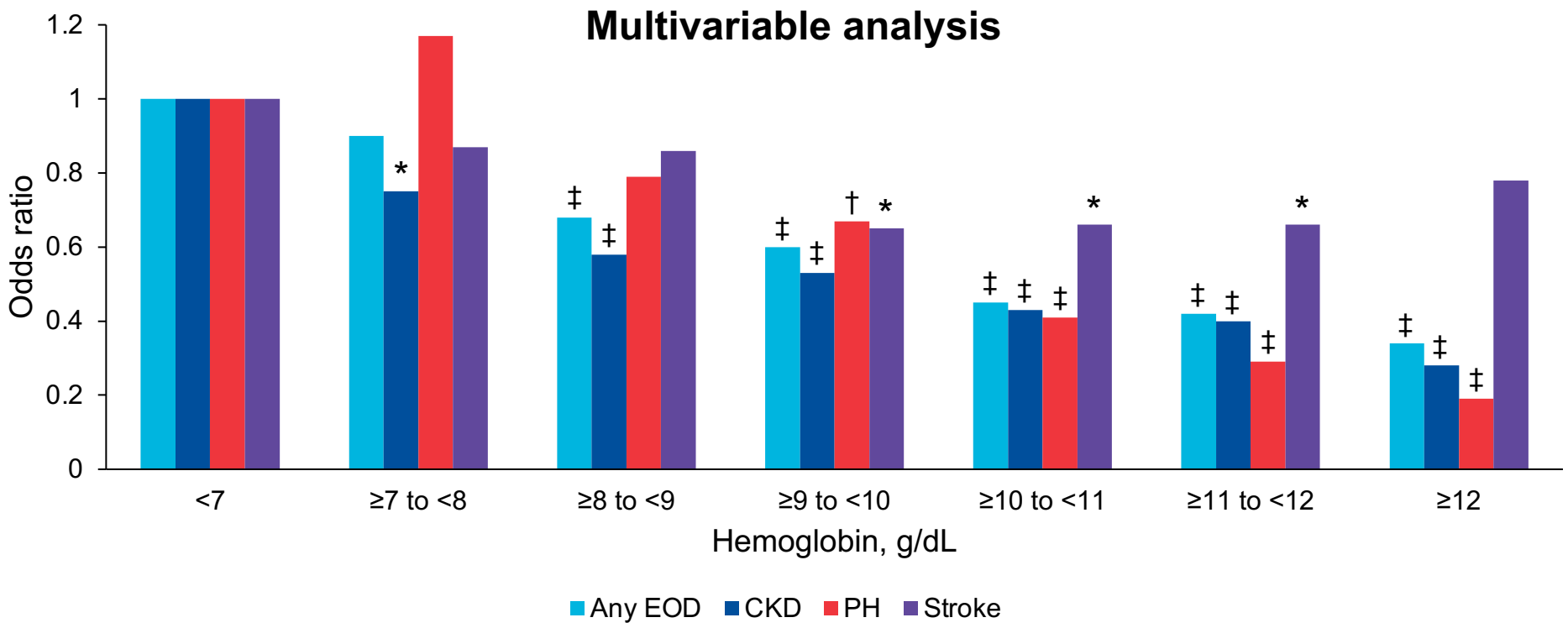
Higher Hb Levels Were Significantly Associated with Reduced Odds of Developing EOD

- A total of 17,034 patients with SCD aged ≥12 years were identified (mean age, 37.8 years; 36.9% male), contributing 44,555 observations of Hb levels (mean [SD], 9.7 [1.9] g/dL).



*P<0.05, †P<0.001 vs Hb <7 g/dL.
CKD, chronic kidney disease; EOD, end-organ damage; Hb, hemoglobin; PH, pulmonary hypertension; SCD, sickle cell disease.

Higher Hb Levels Remained Associated with Reduced Odds of Developing EOD After Controlling for Age, Gender, Insurance Type, and History of EOD and SCD Complications



*P<0.05, †P<0.01, ‡P<0.001 vs Hb <7 g/dL.
CKD, chronic kidney disease; EOD, end-organ damage; Hb, hemoglobin; PH, pulmonary hypertension; SCD, sickle cell disease.

Increased Age, Public Insurance, Concurrent EOD, and SCD-Related Complications Were All Associated with Increased Odds of Developing EOD

Multivariable analysis

Other variables	Any EOD	CKD	PH	Stroke
Sex, female (male=1)	0.81‡	0.67‡	0.83*	1.29†
Age, years (12 to 17 years=1)				
18 to 34	3.60‡	4.56‡	10.49‡	1.21
35 to 49	5.29‡	6.72‡	14.56‡	1.78†
50 to 64	7.77‡	12.80‡	17.28‡	1.98†
≥65	10.36‡	19.07‡	16.21‡	2.77‡
Insurance (commercial=1)				
Medicare and Medicaid	1.83‡	1.72‡	1.58‡	2.66‡
Medicare	1.49‡	1.68‡	1.03	1.60‡
Medicaid	1.62‡	1.83‡	1.07	2.00‡

Other variables	Any EOD	CKD	PH	Stroke
Concurrent EOD				
CKD	0.49‡	N/A	1.31†	1.32*
PH	1.15	1.67‡	N/A	0.93
Stroke	0.95	1.30*	1.10	N/A
SCD-related complications (no history of complication=1)				
Cardiovascular disease	1.82‡	2.01‡	1.92‡	1.66‡
Hepatic disorders	1.22†	N/A	N/A	1.59‡
Pulmonary disorders	1.30‡	1.20*	1.56‡	N/A
Other disorders	1.39‡	1.17*	1.65‡	1.74‡

*P<0.05; †P<0.01; ‡P<0.001.
N/A denotes variables that were not relevant or did not meet stepwise regression criteria (P<0.10).
CKD, chronic kidney disease; EOD, end-organ damage; PH, pulmonary hypertension; SCD, sickle cell disease.

Conclusions

In this large-scale, longitudinal analysis, a significant reduction in the risk of new EOD was observed among SCD patients with higher Hb levels.

History of any EOD was significantly correlated with presence of new EOD.

New SCD treatments that can increase Hb levels can potentially offer clinical and economic value.

EOD, end-organ damage; Hb, hemoglobin; SCD, sickle cell disease.

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