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Healthcare Resource Utilization Among Patients With Sickle Cell Disease With Recurrent Vaso-Occlusive Crises in Germany

COLIN KUNZWEILER,[1] CHUKA UDEZE,[1] NANXIN LI,[1] JESSICA BALDWIN,[1] PETRA TUZIN,[1] SEBASTIAN BARTH,[2] CELINE VETTER,[2] SILVIA DOMBROWSKI,[2] ELENA GEORGIADOU-SCHMIDT,[3] ROLAND MEISEL[4]

[1]Vertex Pharmaceuticals Incorporated, Boston, MA, USA | [2]IQVIA Commercial GmbH & Co. OHG, Frankfurt, Germany | [3]Team Gesundheit GmbH, Essen, Germany | [4]Division of Pediatric Stem Cell Therapy, Department of Pediatric Oncology, Hematology and Clinical Immunology, Heinrich-Heine-University, Düesseldorf, Germany

INTRODUCTION

- Sickle cell disease (SCD) is a rare genetic disorder characterized by the expression of abnormal sickle hemoglobin, which leads to a variety of acute and chronic complications[1,2]
- SCD is associated with vaso-occlusive crises (VOCs), which cause debilitating pain, increase the risk of other complications, and can lead to increased mortality[1,3]
- There are varying definitions of VOC in academic literature, with some more recent clinical trials defining VOC as SCD with acute pain crisis, acute chest syndrome, priapism, or splenic sequestration[4,5]
- There are limited data on healthcare resource utilization (HCRU) among patients with SCD who experience recurrent VOCs in Germany

OBJECTIVE

- To determine the HCRU among patients with SCD with recurrent VOCs in Germany

METHODS

Study Design and Database

- A longitudinal, retrospective cohort study design was used to identify patients with SCD in the Betriebskrankenkasse (BKK) statutory health insurance (SHI) records database from January 1, 2010, to December 31, 2019
  - The BKK database includes 6.7 million insured patients (~7% of the national population) and represents the entire SHI insured German population with respect to age, gender, and main diagnosis groups, as well as federal states and health insurance funds expenditures

Patient Identification

- Patients were included in the analysis if they met the following inclusion criteria:
  - Diagnosis of SCD between January 1, 2010, and December 31, 2018
  - At least 2 VOCs per year in any 2 consecutive years
    - A VOC was defined as SCD with acute pain crisis, acute chest syndrome, or priapism
  - At least 12 months of data availability from and including the index date (see definition below)
- Patients were excluded if they met the following exclusion criteria:
  - Evidence of hereditary persistence of fetal hemoglobin or hematopoietic stem cell transplant at any time in their medical records
- The index date was the date of the second VOC record in the second year of 2 consecutive years
- All patients were followed for ⩾12 months from index to a censoring event or the end of the study period (December 31, 2019)

Matched Controls

- Each patient with SCD with recurrent VOCs was exact matched to 5 controls without SCD or transfusion-dependent β-thalassemia from the general population of Germany

Matched Controls (Continued)

- Matching was based on the following criteria: age (in years) at index, sex, and geographic region
- Matched controls were assigned the same index date as their matched patients
- Matched controls were required to have 1 year of data from and including their index date
- Matched controls were followed for ⩾12 months from index to a censoring event or the end of the study period (December 31, 2019)

Study Measures and Analysis

- Descriptive analyses were conducted for patient demographics and HCRU for patients with SCD with recurrent VOCs and matched controls
  - Mean (standard deviation [SD]) values were reported for continuous variables, and frequencies/proportions (n [%]) were reported for categorical variables
- Demographics, including age, sex, and geographic region, were assessed at index
- The rate of HCRU (per patient per year [PPPY]) was calculated during follow-up
- Comparative analyses were conducted for HCRU between patients and matched controls; a Z-test was used for significance testing ($P<0.05$)

Subgroup Analysis

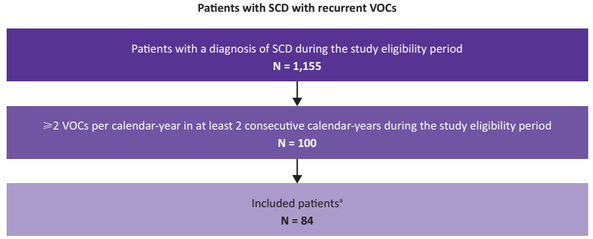
- A subgroup analysis was conducted for HCRU based on the number of VOCs during follow-up (<2 VOCs PPPY or ⩾2 VOCs PPPY)

RESULTS

Patient Demographics

- A total of 84 patients with SCD with recurrent VOCs were identified in the BKK SHI administrative claims database and matched to 420 controls (**Figure 1**)

Figure 1. Patient Attrition



SCD, sickle cell disease; VOC, vaso-occlusive crisis.

[a]Additional inclusion criteria included the following: diagnosis of SCD prior to or at index, at least 1 year of baseline data prior to index, and at least 1 year of follow-up data available from and including index. Patients with evidence of hereditary persistence of fetal hemoglobin or hematopoietic stem cell transplant at any time in their medical records were excluded.

- The mean age of patients with SCD with recurrent VOCs was 40.1 years (SD: 26.0), and 56.0% of patients were male (**Table 1**)
- Demographics between patients with SCD with recurrent VOCs and matched controls were similar (**Table 1**)

Table 1. Baseline Demographics

	Patients With SCD With Recurrent VOCs (N = 84)	Matched Controls (N = 420)
Age (years), mean (SD)	40.10 (25.98)	40.10 (25.98)
Age categories (years), n (%)		
0–11	17 (20.2)	85 (20.2)
12–35	23 (27.4)	115 (27.4)
⩾36	44 (52.4)	220 (52.4)
Sex, n (%)		
Male	47 (56.0)	235 (56.0)
Female	37 (44.0)	185 (44.0)
Follow-up time (years), mean	6.0	6.0

SCD, sickle cell disease; SD, standard deviation; VOC, vaso-occlusive crisis.

HCRU

- Patients with SCD with recurrent VOCs averaged 4.04 VOCs PPPY (SD: 3.85) during follow-up
  - Of the 4.04 VOCs PPPY, 3.98 were SCD with acute pain crisis, 0.02 were acute chest syndrome, and 0.05 were priapism
- Patients with SCD with recurrent VOCs experienced a mean rate of 1.88 hospitalizations, 24.46 outpatient visits, and 24.02 prescriptions (all PPPY) during follow-up (**Table 2**)
- Patients with SCD with recurrent VOCs had significantly higher HCRU than matched controls (**Table 2**)

Table 2. HCRU

HCRU, Mean Rate PPPY (SD)	Patients With SCD With Recurrent VOCs (N = 84)	Matched Controls (N = 420)
Hospitalizations (any type)	1.88 (2.54)	0.28 (0.61)*
Ambulatory[a]	0.81 (1.47)	0.10 (0.40)*
Inpatient[b]	1.07 (1.90)	0.18 (0.36)*
Outpatient prescriptions	24.02 (30.35)	8.67 (12.29)*
Outpatient visits	24.46 (15.32)	12.56 (11.54)*

HCRU, healthcare resource utilization; PPPY, per patient per year; SCD, sickle cell disease; SD, standard deviation; VOC, vaso-occlusive crisis.

[a]Length of stay = 1 day; [b]Length of stay >1 day.

**P<0.0001 between patients with SCD with recurrent VOCs and matched controls (Z-test).*

VOC Subgroup Analysis: HCRU

- Patients with a higher number of VOCs (⩾2 VOC PPPY during follow-up) had higher rates of hospitalizations (0.59 vs 2.71 PPPY) and outpatient prescriptions (17.78 vs 28.06 PPPY) than those with a lower number of VOCs (<2 VOCs PPPY during follow-up) (**Table 3**)

Table 3. HCRU by Number of VOCs Subgroup

HCRU, Mean Rate PPPY (SD)	VOC Subgroups	
	<2 VOCs (n = 33)	⩾2 VOCs (n = 55)
Hospitalizations (any type)	0.59 (0.89)	2.71 (2.90)
Ambulatory[a]	0.10 (0.33)	1.28 (1.72)
Inpatient[b]	0.50 (0.87)	1.43 (2.27)
Outpatient prescriptions	17.78 (14.60)	28.06 (36.74)
Outpatient visits	24.39 (14.10)	24.50 (16.19)

HCRU, healthcare resource utilization; PPPY, per patient per year; SCD, sickle cell disease; SD, standard deviation; VOC, vaso-occlusive crisis.

[a]Length of stay = 1 day; [b]Length of stay >1 day.

LIMITATIONS

- This study used administrative claims data collected for reimbursement purposes and is therefore subject to potential misclassification bias
- There is no standard definition for SCD with recurrent VOCs and thus it is difficult to directly compare this study with other published literature. Although most VOCs in the follow-up period were due to acute pain crises, the study definition of VOC (i.e., SCD with acute pain crisis, acute chest syndrome, or priapism) makes comparability difficult with earlier publications that did not use a similar definition for VOC
  - Splenic sequestration had no ICD-10 code and therefore could not be included in the VOC definition

CONCLUSIONS

- Patients with SCD with recurrent VOCs had significantly higher HCRU (driven by VOCs, hospitalizations, and outpatient visits) than matched controls from the general population in Germany
- A higher number of VOCs was associated with greater HCRU
- Elevated HCRU in patients with SCD with recurrent VOCs highlights the need for innovative therapies that can reduce the number of VOCs and associated HCRU

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AUTHOR DISCLOSURES

This study was sponsored by Vertex Pharmaceuticals Incorporated and CRISPR Therapeutics. CK, CU, NL, JB, and PT are employees of Vertex Pharmaceuticals Incorporated and may hold stock or stock options in the company. SB, CV, and SD are employees of IQVIA and may hold stock or stock options in the company. EGS is an employee of Team Gesundheit GmbH, which received funding from IQVIA for conducting the statistical analysis in this study. RM has received reimbursement for clinical trial participation from Vertex Pharmaceuticals Incorporated; received consulting fees for bluebird bio and Vertex Pharmaceuticals Incorporated; served as an advisory board member for bluebird bio and Vertex Pharmaceuticals Incorporated; and acted as Board Member for the Pediatric Diseases Working Party of EBMT.

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