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Original Article

Health-Related Quality of Life Measurement in Adults With Sickle Cell Disease in Steady State: Experience of One French Reference Center

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Abstract. Sickle cell disease (SCD) is a genetic disease of public health concern. Adult patients face various disease-related complications, which affect their quality of life (QoL). Few studies have examined relationships between these events and health-related (HR) QoL. We conducted a study of 240 adults with SCD seen in steady state at a routine clinic visit over one year. Two self-administered questionnaires were used to determine patients' HRQoL: the sickle cell self-efficacy scale (SCSES) comprising 9 specific items and the unspecific SF-36 scoring system comprising 8 subscales, which construct the physical component summary (PCS) and the mental component summary (MCS). Factors impacting HRQoL were established using univariate and multivariate regression analyses. Participants had a median age of 28 years (Sex ratio male/female 0.61; 68% SS genotype). Most of them had experienced more than one SCD-related complication and more than one affected organ system. A good correlation was established between the SCD-specific and the unspecific scoring systems ($p < 0.0001$). Using the SF-36 scoring system, energy/fatigue, general health, and pain subscales showed the lowest median scores (50, 45, and 56.5, respectively), while physical functioning had the highest median score (75). In univariate and multivariate analyses, hospitalization for SCD complications occurring during the last year preceding QoL evaluation was the main feature impacting HRQoL ($p < 0.001$). Good compliance to hydroxyurea (HU) therapy was associated with higher SCSES ($p = 0.04$) and higher emotional role functioning ($p = 0.03$) scores. The recent occurrence of severe SCD complications mainly influenced HRQoL. Our study suggests that a more effective treatment through better compliance with HU therapy would provide benefit in terms of QoL.

Keywords: : Sickle cell disease; Quality of life; RAND 36; SCSES; Hydroxurea; Complications.

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Introduction. Sickle cell disease (SCD) is a genetic disease that impacts the quality and longevity of life. It is caused by a point mutation in codon 6 of the β-globine chain that results in an amino acid substitution of valine for glutamic acid. SCD is characterized by red-cell sickling under hypoxic conditions, leading to chronic hemolytic anemia, vasculopathy, and vaso-occlusion crisis (VOC), and/or acute chest syndrome (ACS).[1] In contrast to low-income countries, the prognosis of SCD has significantly improved over the last decades in developed countries because of newborn screening, prophylaxis with antibiotics, preventive therapy for strokes, conjugated vaccines, hydroxyurea (HU), evidence-based supportive care, and potentially allogeneic hematopoietic stem cell transplantation. However, patients often still experience painful acute crises as well as chronic, which, in addition to the psychological burden of living, can have a negative impact on patients' health-related quality of life (HRQoL).[2] Most studies on HRQoL have shown that SCD confers a significant burden on patients, including impacts on daily activities, social life, work and education, self-efficacy (SE), and adaptation skills.[3-9] The relationship of SCD complications to diminished HRQoL has been established for frequent sickle pain or opioid usage.[10-13]

The present study utilized a contemporary adult SCD cohort in steady state with the aim of providing insights into the patient-reported impact of SCD on QoL. It provided an opportunity to examine the relationship between social-demographic, clinical, and biological events and patient-reported QoL. In the absence of fully validated SCD-specific questionnaires, most QoL studies have relied on standardized, generic HRQoL assessments. Our main goals were to compare such a scoring assessment with a more specific scoring system and to advance our understanding of factors that are important to improve QoL and function of patients with SCD.

Patients and Methods

Patients. All adult patients (age ≥ 18 years) with SCD (established by hemoglobin electrophoresis, confirmed by genetic analysis when diagnosis was unclear) followed at the Constitutive Reference Center of our University Hospital for major SCDs, seen in steady phase at a routine clinic visit from April 2023 to May 2024, were systematically invited to participate in this prospective study. Overall, 240 successive patients entered the study. All participants were informed about the aims of the study and gave non-opposition consent to anonymous data collection and analyses. The study was approved by an institutional scientific committee (MR004, RNIPH 25-5126) and conducted in accordance with the guidelines set by the Declaration of Helsinki. Four patients (1.6%) did not return the questionnaire or failed to complete it. Therefore, 236 patients were analyzed. Steady state was defined as free of clinical complications, including vaso-occlusive complications or any acute exacerbations, at the time of consultation.[14] People with sickle cell trait (AS) were excluded. Analyzed patients had baseline data on their disease characteristics abstracted from their medical records. Demographic characteristics included: age, gender, body mass index (BMI), and employment. Clinical characteristics included: antecedents of serious SCD events (VOC, ACS, organopathies), current treatments, SCD-related complications since last consultation (6 months), and interval of time from last acute SCD complication requiring hospitalization to the present consultation. Biological parameters included SCD genotype (SS, SC, $S\beta^0$, $S\beta^+$, others), hemoglobin (Hb) level, mean corpuscular volume (CVM), ferritin and vitamin D levels, polymorphonuclear neutrophils (PMN) count, and HbF percentage for patients treated with HU. BMI was calculated as weight (Kg)/height^2 (m^2) and categorized as underweight (<18.5), normal weight (18.5-25), overweight (>25-30), and obese (>30). Anemia was defined as moderate with Hb level between 100 g/L and 70 g/L, and severe with Hb level less than 70 g/L.[15] Patients were stratified as either on HU (defined as having received HU for a minimum of 3 months), chronic transfusion therapy (receiving current monthly exchange or simple transfusions ongoing for a minimum of 6 months), other SCD-specific treatments, or treatment naïve (not on any SCD-specific modifying therapy). Good compliance with HU therapy was arbitrarily defined by HbF > 15% at the time of consultation.

QoL measurement. Two questionnaires were given simultaneously for QoL measurement: (i) the 36-item short-form Health Survey (SF-36) questionnaire, developed by RAND Health, a universally accepted tool for assessing HRQoL of many chronic diseases; and (ii) the sickle cell self-efficacy scale (SCSES), considered as a tailored disease-specific questionnaire.

Short-form health survey SF-36 (RAND 36-item). The SF-36 version 2.0 (RAND 36-item) is a non-disease-specific measure of HRQoL. The RAND 36-item, adapted to the pace of consultations, comprises 36 items with eight subscales: physical functioning (10 items), physical role functions (4 items), bodily pain (2 items), and general health (5 items) which construct the physical component summary (PCS), and emotional role functioning (3 items), vitality (4 items), mental health (5 items), and social functioning (2 items) which construct the mental component summary (MCS).[16-18] PCS and MCS scores were calculated as means of their own subscales. Furthermore, one item scores the patient's health estimation compared to his health status one year

ago, ranging from "much worse" to "much better". Scores of the various parts of the questionnaire are transformed into the range of 0 to 100. Higher scores indicate better QoL, and lower scores indicate poor QoL.

Sickle cell self-efficacy scale (SCSES). The SCSES comprises 9 items that ask the respondents to rate their confidence in their ability to manage their SCD, control SCD-related pain, engage in activities of daily living while living with SCD, and manage emotions/frustrations related to living with SCD.[3] The patients' responses were rated on a 5-point Likert scale ranging from 1 ("not sure at all") to 5 ("completely sure"). The overall score of the scale varies from 9 to 45, and a higher score indicates better SE. The score of the scale is categorized into three levels: low SE (9 – 20.99), moderate SE (21 – 32.99), and high SE (33 – 45).

Statistical analysis. All evaluation parameters were subjected to a descriptive analysis. The quantitative variable evaluation parameters were described using position parameters (mean or median) and dispersion (standard deviation (SD), inter-quartile range (IQR)). The qualitative variable evaluation parameters are shown in the form of numbers and frequency for each modality. Independent t-test and one-way ANOVA were used to compare the mean score of the PCS, the MCS, and the SCSES in terms of dichotomous demographic, clinical, and therapeutic variables. Differences among categorical variables were compared by the χ^2 test.

Regarding continuous variables, the threshold chosen for the analyses was often the median value. In this setting, median PCS and MCS scores were used as cut-offs to individualize higher and lower scores. The significant variables, in addition to PCS and MCS scores, were entered into a regression model as independent variables. Independent determinants of HRQoL were established using multivariate regression models. Estimated hazard ratios (HRs) are reported as relative risks (RR) with 95% confidence intervals (CI). The statistical significance cut-off was set at a p-value < 0.05. All computations were run using the BMDP statistical Software (BMDP Statistical Software, Los Angeles, CA).

Results

Social-demographic, biological, and clinical characteristics of patients. A total of 240 participants with SCD entered the study. Of the enrolled patients, 236 individuals completed the questionnaire and were analyzed. Table 1 provides the demographic characteristics and an overview of the disease and treatment characteristics of the analyzed cohort. The median age was 28 years (range: 18 – 75 years). The cohort included 160 SCD patients with genotype SS (68%), 49 with genotype SC (21%), 14 with $S\beta^0$ thalassemia (6%), 11 with $S\beta^+$ thalassemia (4%), and 2 with others (1%). Main clinical and biological features at the time of QoL evaluation are indicated in **Table 1**. Most patients had experienced more than one SCD-related complication and more than one affected organ system. The prior occurrence of acute VOC was the most common complication (94%), followed by organopathies (66%) and ACS (39%). Among organopathies, gall bladder disease was the most frequent (33%), followed by bone complications (19%), vascular complications (12%), retinopathy (14%), and renal complications (5%). Eleven percent of patients had a prior splenectomy. Seventy-four patients (31%) experienced one hospitalization for SCD complication during the last 6 months. All 74 patients presented VOC complicated by ACS in one case or organopathy in 3 cases. Regarding therapy at the time of consultation, 60% of participants (142 patients) were taking HU. Twenty patients (8%) followed a transfusion program, 16 (7%) received erythropoietin (EPO), and 13 (5%) received iron chelating therapy. Twenty-three patients (9%) participated in investigational trials testing novel agents, including endari (L-glutamine), pyruvate kinase activators, voxelotor, or crizanlizumab.

Health-related quality of life of the patients. **Table 2** shows the median and mean scores and IQR of the 236 patients according to SCSES and RAND SF-36 with its various domains of HRQoL. With the SCSES, 29 patients were classified as low SE (12%), 133 as moderate SE (56%), and 71 as high SE (30%). Three patients did not fill out the SCSES questionnaire. Regarding the RAND SF-36 variables, the lowest scores were in energy/fatigue (mean 48.5 ± 20.6 SD) and general health (46.5 ± 22.6), followed by pain (53.6 ± 26.2). The highest score was in physical functioning (71.1 ± 23.9). Overall, the mean MCS score was 60.0 ± 21.0, and the mean PCS score was 56.2 ± 22.1.

Participants evaluated their current health status compared to the previous year. Forty-eight subjects (20%) rated their general health as somewhat worse or much worse than the previous year, while 90 (38%) indicated that health status did not change, and 98 (42%) that it was better or much better.

Relationships between the used HRQoL scales, SCSES, PCS, and MCS RAND SF-36 subscales were highly correlated ($p < 0.0001$). SCSES and SF-36 subscales also correlated strongly with patients' estimated current health status compared to the previous year ($p < 0.0001$) (**Figure 1 A-D**).

Associations between patient-reported QoL and demographic, disease, and treatment characteristics. Demographic and clinical variables of SCD patients according to PCS, MCS, and SCSES were detailed in **Table 3**. In univariate analyses, iron chelating therapy

Table 1. Characteristics of the 236 patients included in the analyses.

Characteristics	Value
Sex	
Male	90 (38%)*
Female	146 (62%)
Age (years)	28 (18 – 75)**
Job status	
Employed/Student	161 (68%)
Unemployed	75 (32%)
SCD genotype	
SS	160 (68%)
SC	49 (21%)
Sβ-Thal^0	14 (6%)
Sβ-Thal$^+$	11 (4%)
Other***	2
Prior history	
VOC	53
ACS	4
Org	5
VOC/ACS	21
VOC/Org	83
ACS/Org	2
VOC/ACS/Org	65
BMI	
Underweight	33 (14%)
Normal weight	159 (67%)
Overweight	35 (15%)
Obesity	9 (4%)
Biological variables	
Hb (g/L)	96 (54 – 142)
HbF (%)	9.6 (0.1 – 44.1)
MCV (fL)	83.2 (54.1 – 130.2)
PMN (G/L)	3.8 (0.8 – 12.2)
CRP (mg/dL)	3.7 (0.1 – 172)
Vitamin D (nmol/L)	49 (4 – 109)
Ferritin (ng/mL)	95 (6 – 390)
Current treatment	
HU	142 (60%)
EPO therapy	16 (7%)
Transfusion	20 (8%)
Iron chelation	13 (5%)
Hospitalization during the last 6 months	74 (31%)
Time between consultation and last hospitalization (months)	14.5 (0.2 – 364.5)

* Number of patients (%); ** Median (range); *** includes one patient with hemoglobin SD-Punjab and one patient with hemoglobin SO-Arab. Abbreviations: ACS, acute chest syndrome; CRP, C-reactive protein; EPO, erythropoietin; Hb, hemoglobin; HU, hydroxyurea; MCV, mean corpuscular volume; Org, organopathy; PMN, polymorphonuclear; VOC, vaso-occlusion crisis.

Table 2. Descriptive data of the RAND SF-36 and the SCSES in the 236 SCD patients.

Variables	Mean ± SD	Median (range)	IQR (Q3 – Q1)
RAND SF-36			
Physical functioning	71.1 ± 23.9	75.0 (0 – 100)	35
Physical role functions	52.1 ± 40.5	50.0 (0 – 100)	100
Bodily pain	53.8 ± 26.2	56.5 (0 – 100)	34.37
General Health	46.5 ± 22.6	45.0 (0 – 100)	35
PCS	56.2 ± 22.1	56.8 (3.7 – 100)	35.99
Emotional role functioning	59.3 ± 41.1	66.6 (0 – 100)	66.7
Vitality	48.5 ± 20.6	50.0 (0 - 95)	30
Mental health	67.4 ± 18.8	68.0 (8 – 100)	29
Social functioning	64.9 ± 25.3	62.5 (0 – 100)	37.5
MCS	60.0 ± 21.0	61.2 (7.6 – 98.7)	35.02
SCSES	28.6 ± 6.5	28.0 (13 – 45)	9

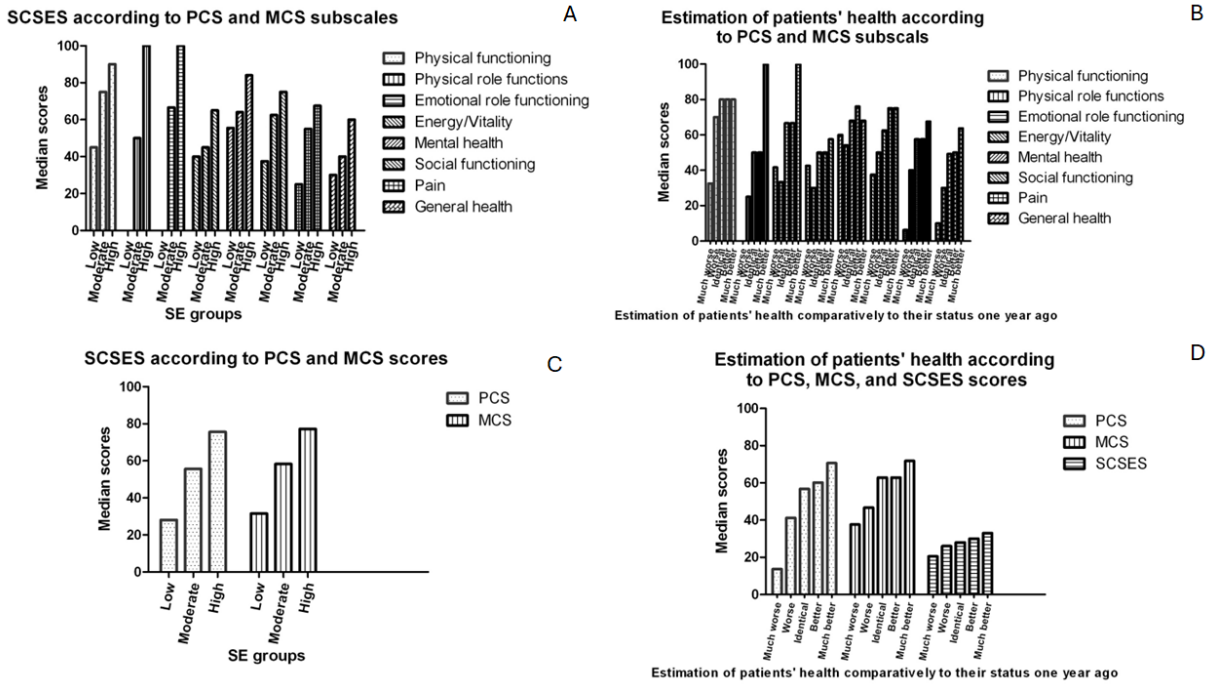

Figure 1. Relationships between the used HRQoL scales. SCSES and PCS and MCS RAND SF-36 subscales were highly correlated ($p < 0.0001$). SCSES and SF-36 subscales also correlated strongly with patient estimated current health status comparatively to the previous year ($p < 0.0001$). (**A**) SE groups according to PCS and MCS subscales, (**B**) Estimation of patients' health according to PCS and MCS subscales, (**C**) SE groups according to PCS and MCS scores, (**D**) Estimation of patients' health according to PCS and MCS scores.

Table 3. Demographic and clinical variables of SCD patients according to three outcome variables: PCS, MCS, and SCSES.

Variables	Number of pts	PCS (Mean ± SD)	MCS (Mean ± SD)	SCSES (Mean ± SD)
Age				
≤ 29 years	120	59.9 ± 20.5	61.1 ± 19.8	29.8 ± 5.5
> 29 years	116	52.3 ± 23.2	58.8 ±22.1	27.4 ± 7.1
Sex				
Male	90	61.4 ± 21.8	62.0 ± 21.1	29.3 ± 6.2
Female	146	52.9 ± 21.8	58.7 ± 20.9	28.1 ± 6.6
Job status				
Employed/Student	161	57.0 ± 21.9	60.4 ± 20.3	29.0 ± 6.1
Unemployed	75	54.3 ± 22.6	59.0 ± 22.5	27.7 ± 7.1
SCD genotype				
SS	160	54.4 ± 23.1	59.2 ± 20.8	28.3 ± 6.2
SC	49	61.0 ± 18.1	63.1 ± 20.4	28.8 ± 7.2
$S\beta^0$	14	58.2 ± 20.2	61.5 ± 21.1	31.2 ± 6.0
$S\beta^+$	11	56.8 ± 27.3	56.0 ± 28.5	28.1 ± 7.9
BMI				
Underweight	33	53.3 ± 21.5	58.7 ± 24.0	27.3 ± 7.1
Normal weight	159	57.2 ± 21.6	59.8 ± 19.7	28.9 ± 5.8
Overweight	35	54.6 ± 26.1	60.1 ± 22.7	28.3 ± 7.8
Obesity	9	53.9 ± 19.7	66.2 ± 26.2	29.0 ± 9.4
Transfusion program				
Yes	20	47.4 ± 23.0	55.8 ± 21.5	26.4 ± 7.2
No	216	57.0 ± 21.9	60.3 ± 20.9	28.8 ± 6.4
HU therapy				
Yes	142	53.7 ± 22.5	57.5 ± 20.7	28.2 ± 6.1
No	94	59.8 ± 21.2	63.7 ± 20.9	29.3 ± 6.9
Iron chelating therapy				
Yes	13	43.6 ± 21.0	57.9 ± 20.6	24.9 ± 6.5
No	223	56.9 ± 22.0	60.1 ± 21.0	28.8 ± 6.4
Epo therapy				
Yes	16	45.8 ± 24.7	52.3 ± 21.4	26.0 ± 7.5
No	220	56.9 ± 21.8	60.5 ± 20.9	28.8 ± 6.4
Hospitalization during the last 6 months				
Yes	74	46.7 ± 20.4	53.6 ± 19.8	27.2 ± 6.0
No	162	60.4 ± 21.6	62.8 ± 21.0	29.3 ± 6.5

Abbreviations: BMI, body mass index; EPO, erythropoietin; HU, hydroxyurea; pts, patients; SCD, sickle cell disease.

was associated with lower PCS scores (p = 0.04), and MCV < 100 fL with lower MCS scores (p = 0.01). Treatment with a novel agent was correlated with both lower PCS and MCS (p = 0.04). In addition, Hospitalizations for SCD complications during the last 6 months and the last year before consultation were significantly associated with lower PCS (p < 0.0001 and p = 0.0001, respectively) and MCS (p = 0.01 and p < 0.0001, respectively) scores. Results are detailed in **Table 4A**.

Multiple regressions were performed to examine the relationship between SCD-specific variables and PCS and MCS SF-36 scores. **Table 4B** presents the findings from multivariate analysis. Hospitalization during the last year remained the main feature significantly associated with PCS (p = 0.0001) and MCS (p = 0.001) scores.

Table 4. Characteristics significantly associated with PCS and MCS scores: results of the univariate (A) and multivariate (B) analyses.

(A) Feature	**PCS < 56.8***	**PCS > 56.8**	**P value**
Iron chelating therapy	8%	2%	0.04
Investigational treatment with novel agent	13%	6%	0.04
Hospitalization during the last 6 months	41%	21%	< 0.0001
Hospitalization during the last year	57%	31%	0.0001
Feature	MCS < 61.2*	MCS > 61.2	P value
Investigational treatment with novel agent	14%	6%	0.04
Hospitalization during the last 6 months	39%	24%	0.01
Hospitalization during the last year	55%	33%	< 0.0001

* Median PCS and median MCS were used as cut-off.

(B) Feature	**HR**	**95% CI**	**P value**
Relationship with PCS score*			
Hospitalization during the last year (yes *vs* no)	0.34	(0.20 – 0.60)	0.0001
Investigational trial testing a novel agent (yes *vs* no)	0.35	(0.12 – 0.95)	0.03
Relationship with MCS score*			
Hospitalization during the last year (yes *vs* no)	0.41	(0.24 – 0.71)	0.001

* Median PCS (56.8) and median MCS (61.2) were used as cut-off. Multivariate analyses included the following factors with either PCS or MCS: hospitalization during the last year, hospitalization during the last 6 months, participation to an investigational trial testing a novel agent. Factors significant in univariate analyses but with many missing data were not included.

Impact of HU therapy on patient-reported QoL. One hundred and forty-two patients received HU at the time of the consultation. Median dose was 18 mg/Kg/day and median time of administration was 71.9 months (range: 3.1 – 382.4 months). In this patient subset, SCSES remained strongly correlated to PCS and MCS RAND SF-36 subscales (p = 0.001 and p = 0.01, respectively). Both SCSES and SF-36 subscales also correlated strongly with patients' estimated current health status compared to the previous year (p = 0.03, p = 0.01, and p = 0.001, respectively). Demographic, therapeutic, and clinical variables associated with PCS and MCS scores were similar in the HU-treated population as in the general patient population.

When considering patients with good compliance to HU therapy defined by HbF > 15%, a significant association was demonstrated with the higher SE group (p = 0.04), and with higher emotional role functioning scores (p = 0.03) of the RAND SF-36. Patients displaying a good compliance to HU therapy were also associated with higher Hb level > 100 g/L (31% *vs* 13%; p = 0.04), MCV > 100 fL (60% *vs* 7%; p < 0.0001), and ferritin > 95 ng/mL (89% *vs* 45%; p < 0.0001).

Discussion. With advances in treatment for SCD, the life expectancy has significantly increased in high-income countries over the last decades, leading to an increased prevalence of mature adults who should deal with repeated SCD complications that may seriously affect their QoL. Although QoL evaluation is a cornerstone in hematological diseases, it is rarely considered as such and is often seen as a secondary endpoint. However, a

better understanding of patient experience and their QoL, especially under treatment, is essential in promoting health and well-being. In this setting, all therapeutic approaches should answer two major questions: "How long can I live without any severe complication of my disease?" and "with what impact on my QoL?"

Available data from the patient viewpoint regarding the SCD impact on QoL remains relatively limited. Most of them have relied on standardized, generic HRQoL assessments, such as the 36-Item Short-Form Health Survey (SF-36).[19-21] These studies have shown that SCD patients still experience very poor HRQoL. However, these generic scales are questionable. They do not consider SCD-specific symptoms and are not comprehensive assessments of all aspects of patients' lives. They may therefore underestimate the burden of illness of SCD. In our study, we first compared the unspecific SF-36 scoring system with the more specific SCSES score. Although this last one questioned more disease-specific points, it also has imperfections and did not explore the physical and mental components of QoL as deeply. Despite these imperfections, the good correlation observed among the two scoring systems strengthened the value of each questionnaire and tended to validate previous published data using the SCD-unspecific scoring system.

Previous studies found that pain impairs health status and QoL more than any other SCD-related complication.[19,22] They reported that SCD did not have negative effects on the emotional and social well-being of the patients,[12,21,22] suggesting a patient adaptation to their chronic disease with a tendency to focus more on the positive experience of the disease.[21] Strong religious beliefs in African populations have been put forward to partly explain this fact.[20] It has also been shown that access to good healthcare services improves the QoL by reducing the frequency of bone pain crises, suggesting that more effective management of persistent pain could improve the QoL. The level of income has also been shown as an independent determinant of QoL.[21,23]

Our findings identified several disease and treatment characteristics that were significantly associated with QoL. In contrast with previous reports,[12,21,22] the main factor associated with patient QoL in our series was directly dependent on the expression of the patient's chronic disease requiring a recent hospitalization for severe SCD complications. Certainly, hospitalization was always associated with VOC and, therefore, pain, but pain was not the primary reason for patient complaints. While SCD genotype is often considered a main determinant of disease severity, SCD genotype was not associated in our study with any HRQoL subscales, which was partly consistent with previous findings. In other studies, HRQoL was not associated with genotype except for the vitality subscale.[12] However, the direction of the statistically significant association between vitality for SS/Sβ^0 thal *vs* SC/Sβ^+ thal was opposite of what would have been expected, with the more severe genotypes being associated with better vitality, suggesting that patients with severe genotypes tended to be more compliant with hospital visits and treatment. Of note, a recent large study reported that the SC genotype was more clinically severe than previously recognized.[24,25] An unexpected finding in our study was the association between lower PCS and MCS scores and patient participation in investigational trials testing novel agents. This relationship with lower scores cannot be explained by potential treatment side effects, given the heterogeneity of tested molecules. It was more likely due to patient apprehension, fears, and anxiety caused by the administration of unknown molecules. Treatments in this patient population are often subject to reluctance, leading to poor compliance with therapy. This reluctance was also seen with a classic treatment such as HU therapy. Indeed, only 41% of patients from our series achieved correct percentages of HbF, signifying good compliance with treatment, generally confirmed by a good correlation with higher MCV values, while all were supposed to receive a regular dose of HU. Good observance of HU doses was associated with higher SE scores and with higher emotional role functioning scores, suggesting less anxiety and depressive tendencies. Previous studies showed better physical functioning in adults with SCD who were taking HU compared to those who were not.[26,27] HU significantly improves pain outcomes, reduces the occurrence of SCD complications, decreases healthcare costs, and improves HRQoL.[28-31]

Despite interesting findings, a number of limitations should be noted in our study. Subject selection could have been biased toward less symptomatic individuals as recruitment was targeted to stable individuals seen in programmed consultation or day care unit hospitalization for regular health check, while the questionnaire was not proposed at the time of hospitalization for any SCD complications. Some important factors were not assessed, such as measurement of protein-energy intake and micronutrient levels, the deficiency of which was shown to increase SCD severity and hospitalizations, and to reduce HRQoL.[32] Furthermore, some studied subpopulations were too small to allow accurate statistical analyses and should only be interpreted with caution. HU compliance was arbitrarily defined and voluntary, quite simplistic. It may be affected by inter-individual variability. A more complex and likely more accurate definition of HU compliance involving additional factors to HbF was not selected because it would lead to too small subgroups. Although not representing many patients (4 patients), another potential bias was the need for the subjects included to be able to understand and answer the questionnaire, excluding therefore patients not fluent in the French language.

Conclusions. Overall, our study confirmed the utility of the QoL questionnaire, whatever it was, to estimate the physical and mental components of patients with SCD. QoL in patients, although in steady state, remained relatively poor, with median PCS and MCS only around 60% and median SCSES score in the moderate group. Fatigue and pain remained the most affected subscales. Negative points were related to chronic manifestations of the disease: recent hospitalizations impacted HRQoL severely, as also did chronic features associated with severe anemia. The most important point was the favorable impact of HU therapy on QoL when correctly taken. This encourages us to monitor HU therapy more closely and to encourage patients to comply with their treatment. Our study suggests that a more effective management of the disease, notably in terms of compliance with the prescribed therapy, could substantially improve the QoL for adults with SCD. Validation on a larger prospective series is warranted.

Author contributions. Giovanna Cannas contributed to the study conception and design, performed statistical analyses, interpreted the data and wrote the manuscript. Giovanna Cannas, Solène Poutrel, Emilie Virot, Manon Marie, Alexandre Guilhem, and Amal El-Kanouni took care of patients. Richard Bourgeay provided technical support. Marie-Grace Mutumwa and Mohamed Elhamri performed data collection. Arnaud Hot critically reviewed the manuscript. All authors read and approved the final manuscript.

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