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Fatigue and Depression Predict Reduced Health-Related Quality of Life in Childhood-Onset Lupus

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Summary

We aimed to identify risk factors for persistently reduced health-related quality of life (HRQoL) in childhood-onset lupus (cSLE) and describe a risk profile for persistently reduced HRQoL. At a tertiary rheumatology clinic, 50 cSLE patients were assessed twice approximately six months apart. Measures of disease activity and patient-reported measures of HRQoL, pain, depressive symptoms, anxiety and disability were collected at each visit. At visit 1 and 2 respectively, clinically relevant fatigue was present in 66% and 56% of patients; clinically significant depressive symptoms in 26% and 24%; and clinically significant anxiety in 34% and 28%. Poorer HRQoL at follow-up was significantly predicted by higher fatigue and depressive symptoms at the initial visit. Using clinically relevant cutoffs for fatigue and depressive symptoms, patients were assigned to Low (n=27) or High Risk (n=23) groups. A profile of significantly greater pain, anxiety and coping difficulties was seen in the High Risk group. Routine assessment of fatigue and mood symptoms in youth with cSLE could be helpful in identifying those at risk for persistently poor

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HRQoL. Integration of behavioral interventions to address fatigue and mood symptoms into medical care for such patients may be beneficial but more research in this area is needed.

Keywords

childhood-onset systemic lupus erythematosus; depression; fatigue; health-related quality of life

INTRODUCTION

Childhood-onset systemic lupus erythematosus (cSLE) accounts for 15–20% of all patients with SLE, with a prevalence of 3.3–8.8 per 100,000 children^{1, 2}. While survival for these patients has significantly improved, cSLE remains a chronic, episodic health condition which can critically influence a child's psychosocial development. Health-Related Quality of Life (HRQoL) encompasses physical, psychological and social functioning domains². A growing understanding of the variability in individual responses to similar conditions has researchers looking further than traditional clinical and laboratory measures to improve outcomes. In pediatric patients with cancer and other chronic diseases, poor physical health, child emotional problems, and caregiver baseline stress have emerged as HRQoL correlates which may be amenable to intervention^{3, 4}.

Research suggests that SLE is associated with decreased HRQoL compared to healthy norms, though measures of disease activity and organ damage often prove to be poor indicators of patients' reports of impaired HRQoL^{5, 6}. Specifically, results from a prior cross-sectional investigation by our research group indicated that even with well controlled disease activity and low disease damage, a sub-group of cSLE patients reports substantial pain, fatigue and to a lesser extent anxiety, which negatively impacts their HRQoL⁶. In adult patients with SLE, older age, presence of fatigue and co-morbid neurological or psychiatric disorders, particularly depression or anxiety have been found to be predictors of lower HRQoL⁵.

At present, screening to evaluate HRQoL of cSLE patients is uncommon in clinical care; therefore, children with chronically poor HRQoL are not being identified. Assessment of patient reported outcomes over time offers an opportunity to proactively identify those at risk for poor HRQoL and improve the care of cSLE patients by providing appropriate referrals and tailored care better matched to the needs of individual patients.

The objectives of this study were to 1) assess disease characteristics, fatigue, pain, psychological symptoms and HRQoL in patients with cSLE at two visits over a 6-month period, 2) identify significant predictors of reduced HRQoL at follow-up, and 3) use the most relevant predictors to create a risk stratification (High and Low Risk) for persistently poor HRQoL of adolescents with cSLE and describe the profile of disease and psychosocial characteristics for each of these groups. Our primary hypothesis was that higher levels of fatigue, pain and mood (depressive) symptoms at visit 1 would predict lower HRQoL at visit 2 six months later.

METHODS

Patient population

In an initial cross-sectional study, we reported on a convenience sample of 60 children and adolescents with cSLE who were receiving medical care at the Cincinnati Children's Hospital Medical Center (CCHMC) rheumatology clinic ⁶. Fifty of the 60 patients who were approached at subsequent clinic visits agreed to participate in follow-up assessment during their medical clinic appointment approximately six months later. Patients aged 8–20 years were eligible for participation provided they fulfilled the revised American College of Rheumatology Classification Criteria for SLE by age 18 years ⁷. Patients with cSLE were excluded from participation if they had history of co-morbid chronic disease besides cSLE that might impact HRQoL. Those previously diagnosed with depression or anxiety were not excluded. The study was approved by the institutional review board, and informed consent (if >18 years of age) or assent was obtained from study participants and parents/primary caregivers (of minors).

Patient reported measures

Patients completed self-report questionnaires of fatigue, pain, pain catastrophizing, depressive symptoms, anxiety, HRQoL and functional disability. Though certain measures were only validated for use in the pediatric age range up to 18 years old, the same measures were used in 19–20 year olds for consistency in this follow up study.

Fatigue—The Pediatric Quality of Life Inventory Multidimensional Fatigue Scale (PedsQL-FS) is an 18-item inventory designed to measure fatigue in pediatric patients over the previous month. It is comprised of three domains: general fatigue, sleep/rest fatigue and cognitive fatigue, with six items for each subscale. Items are rated on a 5-point Likert scale (0 = never, 1 = almost never, 2 = sometimes, 3 = often, 4 = almost always). From the raw scores, a summary score of 0 to 100 can be calculated with a lower score representative of increased fatigue. Internal reliability for child report is high, $\alpha = 0.95$ ⁸ and in this study the Cronbach α was 0.92. In addition to the PedsQL-FS, patient-reported presence of generalized fatigue in the last seven days was obtained (as a dichotomized variable – “yes” or “no”) as part of a checklist of symptoms in a standard medical review of systems.

Pain—The Brief Pain Inventory (BPI) is a 10-item inventory, which enquires about pain duration, location, intensity, interference and frequency ^{9, 10}, and includes a pain numeric rating scale (pain-NRS; 1 – 10; 0= no pain) to indicate average pain intensity in the last week with higher number representative of higher pain, and clinically relevant pain indicated by pain-NRS is defined as > 3 out of 10 ^{11, 12}.

Pain Catastrophizing—This refers to exaggerated worry about the negative consequences of pain, perceived lack of control over symptoms and an inability to cope with pain ¹³. The Pain Catastrophizing Scale (PCS) for children is a validated scale consisting of 13 items all rated on a 5-point Likert scale (0 = not at all, 1=mildly, 2 = moderately, 3 = severely, 4 = extremely) which measures negative, catastrophic thoughts about pain. The PCS items can be grouped in three subscales: rumination (four items), magnification (three items), and

helplessness (six items). A PCS summary score (range 0 to 52) can be calculated from the sum of the item scores, with higher summary scores representative of increased catastrophizing. PCS summary scores can be interpreted as follows: low (0 to 14), moderate (15 to 25), and high (≥ 26) pain catastrophizing^{14, 15}. The internal reliability of the PCS is excellent, $\alpha = 0.93$ ¹⁵ and in this study the Cronbach α was 0.92.

Depressive Symptoms—The Children's Depression Inventory Version I (CDI-I) is a well-validated 27-item measure that assesses mood and depressive symptoms. Each item has three response options that quantify severity of each depressive symptom, and is scored 0, 1, or 2. A higher total score indicates higher level of depressive symptoms with a CDI-I raw score cut-off value of 14 reflecting the presence of clinically relevant depression¹⁶. The internal reliability of the CDI-I is very high, $\alpha = 0.88$ ¹⁷ and in this study the Cronbach α was 0.92.

Anxiety—The Screen for Child Anxiety Related Emotional Disorders (SCARED) is a validated measure consisting of 41 items grouped into five subscales: panic/somatic symptoms, generalized anxiety, separation anxiety, social anxiety, and school phobia and a total sum score greater than or equal to 25 that represents the presence of clinically relevant anxiety. Items are rated on a 3-point scale (0 = not true or hardly ever true, 1 = somewhat true or sometimes true, 2 = very true or often true), with higher score representative of more anxiety¹⁸. The internal reliability for the SCARED total sum score is excellent and ranges from 0.89 to 0.92¹⁸ and in this study the Cronbach α was 0.96.

HRQoL—The Pediatric Quality Of Life Inventory Generic Core scale 4.0 (PedsQL-GC)¹⁹ and Rheumatology Module 3.0 (PedsQL-RM)²⁰, and patient global assessment of health (10-point numerical scale with higher score representative of better health) were completed.

The PedsQL-GC is a self-report tool comprised of 23 items divided among four domains which include: Physical, Social, School and Emotional. Internal reliability for the PedsQL-GC is excellent, $\alpha = 0.89$, and for this study Cronbach α was 0.93. The PedsQL-RM was administered along with the PedsQL-GC and probed HRQoL domains relevant to children with rheumatic diseases. The PedsQL-RM consists of 22 items grouped into five domains which include: Pain and Hurt, Daily Activities, Treatment, Worry and Communication. The internal reliability for the PedsQL-RM ranges from 0.75–0.86 and for this study Cronbach α was 0.93. For both the PedsQL-GC and -RM, items are rated on a 5-point scale (0 = never, 1 = almost never, 2 = sometimes, 3 = often, 4 = almost always), and from the raw scores a summary score of 0 to 100 is calculated with higher score representative of better HRQoL²⁰.

Disability—The Functional Disability Inventory (FDI) is a 15-item measure that assesses difficulty in physical and psychological function, and perceived activity limitations²¹. The FDI has a 5-point scale (0 = no trouble, 1 = a little trouble, 2 = some trouble, 3 = a lot of trouble, 4 = impossible), and the total score is comprised of the sum of the item scores. FDI total scores of less than 12 are considered to reflect no or minimal disability, 13 to 29 moderate disability; and greater than 30 severe disability, respectively²². The internal reliability of the FDI ranges from 0.86 to 0.91²³ and in this study the Cronbach α was 0.86.

Physician completed measures

Information collected as part of standard clinical care for cSLE (medications, disease activity, duration and damage) was obtained from the patients' electronic medical record.

Disease activity—The Systemic Lupus Erythematosus Disease Activity index (SLEDAI-2K, range 0 to 105; 0 = inactive disease)²⁴ and the British Isles Lupus Activity Group index (BILAG, disease activity in eight domains – general, mucocutaneous, neurological, musculoskeletal, cardiovascular and respiratory, vasculitis, hematology and renal with alphabetical value that is transformed to numerical score (A = 12, B = 8, C = 1, D = 0, E = 0); 0 = inactive disease) were used to assess disease activity²⁵. Both have been validated in cSLE and the BILAG was added because it contains items that address subjective symptoms that cannot be objectively measured which include, but are not limited to, fatigue, arthralgias and myalgias²⁶. The physician global assessment of disease activity (MD global) was also used.

Damage—Disease damage was evaluated with Systemic Lupus International Collaborating Clinics/ACR Damage Index (SLICC/ACR-DI), range 0 to 47; 0 = absence of damage)²⁷.

Statistical Analysis

Descriptive statistics for continuous variables used means and standard deviation (SD); and for binary and categorical variables frequency and percentage. The means of fatigue (PedsQL-FS), pain (Pain-NRS), psychological variables (SCARED, CDI-I, PCS), HRQoL summary scores (PedsQL-GC, PedsQL-RM), disability (FDI) and cSLE measures (SLEDAI-2K, BILAG, SLICC/ACR-DI, MD global) between visit 1 and visit 2 were compared using paired sample t-tests.

Based on correlation analyses, psychosocial factors (i.e., fatigue, depressive symptoms) at visit 1 that were significantly related to HRQoL at visit 2 were included in the statistical model. Predictors of HRQoL at visit 2 were evaluated using hierarchical regression analysis, after controlling for age and concurrent disease activity. Age and disease measures (SLEDAI-2K and SLICC/ACR-DI) were entered in the first step of the regression analysis. The BILAG and SLEDAI-2K are highly correlated ($r=0.79$, $p<0.001$) and because of the more objective nature of the SLEDAI-2K, the BILAG was not included in the regression analysis. Next, the pain-NRS score (pain) and the PedsQL-FS score (fatigue) were entered into the model, followed by the CDI-I score (depressive symptoms) in the final step of the regression model. Given the strong collinearity between anxiety and depressive symptoms (bivariate correlation 0.66) and to be consistent with the adult SLE literature, anxiety was omitted from the model, while retaining depressive symptoms as the primary indicator of mood symptoms²⁸. Once the significant predictors for lower HRQoL were identified, patients were classified into High and Low Risk groups for impaired HRQoL based on published clinical cut-points for these variables. Descriptive statistics for all measures of disease activity, pain and psychological variables were computed for the High and Low Risk groups at visit 1 and 2.

RESULTS

Population and Demographics

Fifty patients were available and agreed to participate in the second visit at approximately 6 months follow-up, representing 83.3% of the original inception cohort. Table 1 summarizes patient demographics and medications used for treatment during the study. The cohort was 84% female, with 23 (46%) African American, and 23 (46%) Caucasian participants. Participants ranged from 11–20 years with mean age 16.2 (SD 2.5) years. Medication regimens were generally stable between visits. At visit 1 and 2 respectively, 18% and 22% were prescribed anti-depressants. With more systematic screening using patient-reported measures as part of this study, we noted that for those with clinically relevant depressive symptoms, ten out of 13 patients at visit 1 and eight out of 11 patients at visit 2 were not treated with anti-depressants. cSLE activity (SLEDAI-2K, BILAG) was well controlled during the study, and disease damage (SLICC/ACR-DI) was absent in the majority of the patients.

Patient Reported Outcomes at each of the visits

The mean scores and SDs for disease measures, HRQoL variables and psychological variables, with comparison to healthy normative population (if available) or cut-off scores are summarized in Table 2. Clinically significant fatigue (Peds QL-FS) was reported by the majority of the patients at both visits. Clinically significant depressive symptoms and anxiety were reported between 24–34% of the patients during the study. The majority of cSLE patients reported no more than minimal functional disability. While significant improvements in SLEDAI-2K and physician assessment of disease activity were observed between baseline and follow up, HRQoL continued to remain lower than data on healthy norms. Though a small number, boys (n=8) had lower SLEDAI-2K scores, minimal depressive symptoms and better HRQoL as measured by the PedsQL-RM when compared to girls. While not statistically significant, participants 18 years (n=17) had higher SLEDAI-2K scores, and slightly better HRQoL (PedsQL-GC, PedsQL-RM).

Predictors for Low HRQoL

Age, disease activity and pain were not found to be statistically significant predictors of HRQoL measured by PedsQL-GC at follow-up. As summarized in Table 3, the strongest predictive risk factor for low HRQoL at visit 2 was fatigue (measured by PedsQL-FS), which predicted 57% of model variance (R^2 change =0.51; p-value 0.005). Depressive symptoms (measured by CDI-I) were also important predictive risk factors of lower HRQoL at visit 2, and its added consideration in the models increased the variance prediction of model variance to 63% (R^2 change=0.06; p-value 0.009). Standardized beta coefficient and adjusted R square values for the final regression model are presented in Table 3.

Risk categorization

Additional analysis was done to categorize the level of risk for reduced HRQoL at visit 2, based on clinically relevant cut-offs from visit 1 scores of fatigue and depression. The sample was grouped by risk level with the High Risk group defined by clinically relevant

fatigue (PedsQL-FS = 53.9; 2 standard deviations below healthy normative value⁸) and/or depressive symptom score (CDI-I = 14; 75th percentile based on normative values¹⁶). Using this categorical structure, 23 (46%) SLE patients were assigned to the High Risk group and 27 (54%) to the Low Risk group. Descriptive data on disease activity, pain and psychological characteristics of these two groups are provided in Table 4.

Comparison of High Risk and Low Risk Group

As shown in Table 5, patients in the High Risk group were all female, as were 70% of the Low Risk group. There was no significant difference in average disease duration, however patients in the High risk group were older. Patients ranged from newly diagnosed to 10 years of disease. In the High risk group, 30% were diagnosed with cSLE within the last one year, compared to 19% in the Low risk group. Parent factors, notably education level, income and insurance status were similar between both groups. Despite ongoing standard of care of cSLE which did not include any behavioral intervention, those in the High Risk group experienced persistently poorer HRQoL (PedsQL-GC, PedsQL-RM) and increased disability, as well as higher anxiety, pain intensity and pain catastrophizing across time points. Disease activity measures (SLEDAI-2K, BILAG) improved over the study period, while SLICC/ACR-DI scores remained stable. Closer examination of the PedsQL-RM showed that the High Risk group had particularly low scores (more impairment) in the domains of Pain and Hurt, Worry, and Communication, while scores of the Daily Activities and Treatment domains were comparable to those in the Low Risk group (Table 4).

DISCUSSION

To our knowledge, this is the first pediatric study to identify potentially modifiable predictors of impaired HRQoL in cSLE patients. Notably, a sizeable proportion of our cohort had persistently poor HRQoL across the ~6-month time frame of the study, even with medically well-managed disease. Despite the near normative values for depressive symptoms, anxiety and pain for the overall sample of cSLE patients in this study, an important contribution of this study was the identification of a subgroup that demonstrated greater psychosocial difficulties. Results showed that higher levels of fatigue and depressive symptoms were the most important contributors to reductions in HRQoL over the 6-month period. Using brief patient-reported surveys that are easy to administer in a clinical setting, we were able to identify those at High versus Low risk for impaired HRQoL.

A recent prospective international multicenter longitudinal cohort study (n=467) found that higher disease activity and higher damage was associated with lower HRQoL in cSLE patients²⁹. On the other hand in our study, and in line with some earlier studies, disease activity and accumulated damage were not found to highly correlate with HRQoL in cSLE^{5, 6}. This might have been due to the fact that cSLE was well controlled in our study population and disease damage was generally absent. Although we had relatively few males in the sample, similar to the study by Moorthy et al²⁹, female gender appeared to be associated with lower HRQoL. Moorthy et al found HRQoL domains most impacted included Emotional (PedsQL-GC) and Worry (PedsQL-RM)²⁹.

With disease activity well managed, the predictors of impaired HRQoL over time in our cohort were related to fatigue and mood symptoms. Consistent with prior adult and pediatric literature, fatigue was present in the majority of cSLE patients at both visits ^{30, 31}. In adult lupus patients, less fatigue over time was predicted by decreases in depression, supporting the notion that fatigue may reflect mental health more than disease activity ³². With regard to mood symptoms, about one-fourth of this sample reported clinically significant depressive symptoms and about a third of the sample reported clinical elevations in anxiety. Depressive symptoms were found in rates similar to patients with juvenile idiopathic arthritis, however anxiety symptoms were not as high as in patients with juvenile fibromyalgia syndrome ^{33, 34}. In a recent cross-sectional study of cSLE, 34% of the cohort were affected by depression and anxiety symptoms. Patients with depressive symptoms were less likely to visit their primary care providers than those without, and subsequently unlikely receiving mental health treatment ³⁵. In a population based cross-sectional study of adolescents with self-reported rheumatic diseases, depression was reported by 19% of the study participants, as compared to 5% of the healthy controls. Nonetheless there was no difference in rates of contact with a psychologist ³⁶. Greater attention to behavioral and psychosocial aspects is likely needed to provide more comprehensive care for these patients.

Rates of depressive symptoms in our cohort were consistent with an earlier study which reported that about one-third of all cSLE patients have elevated depressive symptoms, though they did not measure use of anti-depressants ³⁷. In our study, approximately one fifth were prescribed anti-depressants at visit 1 and 2. This is double what has been reported for the general population (age >12 years) ³⁸ and may reflect increased recognition of these symptoms in our practice. However, we also noted that a majority of those with clinically relevant depressive symptoms based on patient-reported measures in our study, were not treated with anti-depressants. There are ongoing efforts to encourage primary care providers in the role of screening, intervention and care coordination for adolescent depression ³⁹. Rheumatologists may at times be a cSLE patient's principal provider and this offers an opportunity to address potential unmet mental health needs. It is known that depression in adolescence can have lasting effects into adulthood, predicting a range of mental health disorders in adult life including anxiety disorders, substance-related disorders and bipolar disorder ⁴⁰. Adults with SLE and co-morbid depression and anxiety have associated poorer medication adherence, increased disease activity and lower work productivity ⁴¹. In both adult SLE and children with other chronic conditions, poorer mental health and depression has been associated with increased healthcare utilization ³⁵. Taken together, this suggests recognition of mental health issues prior to adulthood is likely to result in earlier treatment, with potential for improvement of HRQoL, as well as cost of care overall.

In the subgroup analysis, those in the group with impaired HRQoL, which comprised about half the patients, had significantly higher levels of pain, pain catastrophizing and anxiety, with particular concerns in the PedsQL-RM domains of Pain and Hurt, Worry and Communication. These findings indicate that a large subgroup of patients with cSLE have significant psychological symptoms, worry and difficulty coping with their medical condition. In adult SLE patients, prior research has shown that anxiety, low self-efficacy for pain control and pain catastrophizing are all significantly related to physical symptoms and

psychological distress⁴². This study provides evidence that similar to findings in adults, pain, fatigue, emotional and coping difficulties are also common in cSLE.

Our findings affirm prior knowledge that treatment aimed at improving cSLE inflammation and damage alone is not enough to improve HRQoL outcomes. Overall, results suggest that routine assessment of fatigue and depressive symptoms be considered as part of clinical care, to provide early recognition of those cSLE patients at greatest risk for poor HRQoL. This may allow for tailored and targeted interventions to be offered to those particular patients. This is important because adolescent and young adult patients with cSLE report a desire for autonomy in their healthcare but at the same time are uncertain about their own capacity to self-manage an unpredictable disease⁴³. Behavioral approaches such as cognitive behavioral therapy (CBT) have resulted in improved outcomes for patients with arthritis pain⁴⁴ and CBT has also been shown to be effective for improving coping and reducing depressive symptoms in children with chronic pain and fatiguing conditions such as juvenile fibromyalgia^{45, 46}. CBT may be particularly well-suited for this population because it is recognized as an evidence-based treatment for depression^{47, 48} and has been beneficial in improving coping in patients with chronic fatigue⁴⁹. Teaching cSLE patients active and adaptive coping skills to reduce fatigue and depressive symptoms may be a particularly promising approach for those identified as high risk for impaired HRQoL. However, these interventions have not yet been developed in pediatric cSLE populations. Interventions will likely be most effective if barriers to treatment for adolescents, such as perceived stigma and concern about family member response, as well as parent barriers, such as cost and access to care are also addressed⁵⁰.

We note several limitations to the current investigation. The sample of cSLE patients recruited from one pediatric center in the US may limit generalizability of the findings. The majority of participants are adolescents which may limit generalizability of the findings for younger children. Given the pilot nature of this study, we did not correct for multiple comparisons in our data analysis. The main goal was to test potentially important risk factors in impaired quality of life that deserve further study. We recognize that other factors may also play a role, such as sleep quality and life stressors but these were outside the scope of this investigation. The specific contributory factors to fatigue in cSLE are not well understood at this time and this study further underscores the need for additional examination of the mechanisms underlying fatigue in cSLE. Finally, although we don't have data regarding those currently receiving counseling, a pilot study to examine the effect of tailored behavioral intervention and counseling for those found to have poor HRQoL is currently underway.

Nevertheless, the findings of this study clearly highlight the importance of early assessment of potentially modifiable risk factors that may be amenable to intervention. Beginning to address some of these factors in the comprehensive management of cSLE patients would represent a significant step forward in the optimal medical and HRQoL outcomes.

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Demographics and SLE features (n=50)

Table 1

Measure	Mean (SD)	Frequency n [%]
Age, years	16.2 (2.5)	
Female		42 [84%]
Race	African American	23 [46%]
	Caucasian	23 [46%]
	Other	4 [8%]
Ethnicity (Hispanic)		4 [8%]
Disease duration, years	2.7 (2.6)	
Medications (Visit 1/Visit 2)	Prednisone	26 [52%]/23 [56%]
	Mycophenolate	22 [44%]/19 [38%]
	Azathioprine	2 [4%]/2 [4%]
	Methotrexate	3 [6%]/6 [12%]
	Cyclophosphamide	2 [4%]/1 [2%]
	Hydroxychloroquine	48 [96%]/48 [96%]
	NSAID	28 [56%]/34 [68%]
	Antihypertensive	11 [22%]/12 [24%]
	Antidepressants	9 [18%]/11 [22%]
SLEDAI-2K score [*]	4.8 (4.5)	
BILAG score ^{**}	8.0 (8.3)	
SLICC/ACR-DI [†]	0.5 (0.8)	

^{*} Systemic Lupus Erythematosus Disease Activity Index;

^{**} British Isles Lupus Activity Group Index; alphabetical scores converted as follows: A=12, B=8, C=1, D=0, E=0;

[†] Systemic Lupus International Collaborating Clinics/ACR Damage Index

Table 2

Comparison of Visit 1 and 2 Measures in Study Population (n=50)

Mean (SD) n [%] above cut-off	Normative population mean (SD) or cutoff value	VISIT 1	VISIT 2	p- value [†]
Psychological Variables				
Fatigue (PedsQL-FS)	80.5 (13.3)	58.6 (18.9) 33 [66%]	61.2 (21.2) 28 [56%]	0.16
Depression (CDI-I)	9.1 (7.0)	9.1 (8.1) 13 [26%]	8.3 (7.7) 12 [24%]	0.30
Anxiety (SCARED)	17.4 (12.1)	20.2 (16.3) 17 [34%]	17.1 (16.8) 14 [28%]	0.09
Pain Catastrophizing (PCS)	14	17.9 (10.4) 29 [58%]	15.4 (11.9) 23 [56%]	0.13
Pain (BPI Pain-NRS)	4	2.8 (2.5) 20 [40%]	2.3 (2.3) 13 [26%]	0.20
Disease Measures				
SLEDAI-2K	N/A	5.3 (5.2)	4.2 (3.7)	0.03
BILAG	N/A	10.0 (9.5)	6.0 (6.6)	0.001
Physician global assessment of disease activity [0 – 10]	N/A	2.1 (1.8)	1.8 (1.7)	0.04
SLICC/ACR-DI	N/A	0.5 (0.8)	0.5 (0.8)	
HRQoL Variables				
Functional Disability Index (FDI)	12	6.5 (6.6) 8 [16%]	4.8 (5.4) 6 [12%]	0.02
PedsQL-GC	83.9 (12.5)	72.2 (17.8)	76.1 (17.9)	0.03
<i>Physical</i>		72.8 (21.4)	76.4 (20.0)	
<i>Emotional</i>		70.5 (24.6)	73.9 (24.7)	
<i>Social</i>		82.1 (20)	86 (19.8)	
<i>School</i>		63.2 (20.3)	37.9 (22.4)	
PedsQL-RM	84.4 (18.0)	73.2 (19.1)	77.7 (17.3)	0.01
<i>Pain and hurt</i>		65.2 (25.4)	71.1 (21.5)	
<i>Daily activities</i>		90.2 (16.2)	92 (12.9)	
<i>Treatment</i>		79.1 (20.0)	80.9 (17.1)	

Mean (SD) n [%] above cut-off	Normative population mean (SD) or cutoff value	VISIT 1	VISIT 2	p- value [‡]
<i>Worry</i>		61.2 (30.1)	70.0 (29.2)	
<i>Communication</i>		70.3 (30.0)	74.7 (29.0)	

[‡] Denotes use of Student's T-test to determine p-values comparing means at visit 1 and 2

Table 3

Hierarchical regression analyses predicting HRQoL (PedsQL-GC) at visit 2

Predictor Variable	beta coefficient *	p-value	R ² **	R ² change
Step 1			0.06	0.06
<i>Age</i>				
<i>SLICC/ACR-DI</i>	0.14	N/S		
<i>SLEDAI-2K</i>	-0.04	N/S		
Step 2			0.57	0.51
<i>Pain</i>	-0.18	N/S		
<i>Fatigue</i>	0.40	0.005		
Step 3			0.63	0.06
<i>Depressive symptoms</i>	-0.35	0.009		

* Represents the standardized coefficients

** Coefficient of multiple determination (how much model variance is predicted by each step, and then change with each additional step added to the model)

Table 4

Low and High Risk Groups based on Fatigue and/or Depressive symptoms at Time 1

	Low Risk Group n=27		High Risk Group n=23	
	Mean (SD)		Mean (SD)	
	TIME 1	TIME 2	TIME 1	TIME 2
Psychological variables				
Anxiety (SCARED)	14.3 (13.4)	10.7 (11.6)	27.3 (16.8)	24.6 (18.9)
Pain Catastrophizing	13.5 (9.5)	12.5 (10.7)	23.0 (9.2)	18.8 (12.5)
Pain (BPI pain)	2.3 (2.4)	1.7 (1.8)	3.4 (2.6)	3.1 (2.5)
Disease measures				
SLEDAI-2K	4.4 (4.8)	3.7 (3.8)	6.3 (5.6)	4.8 (3.7)
SLICC/ACR-DI	0.59 (0.93)	0.63 (0.93)	0.39 (0.72)	0.39 (0.72)
BILAG	8.0 (7.1)	5.2 (5.5)	12.3 (11.4)	6.9 (7.7)
HRQoL Variables				
PedsQL-GC	80.8 (13.6)	83.5 (13.1)	62.0 (17.0)	67.4 (19.0)
Physical	82.3 (17.2)	83.0 (17.9)	61.7 (20.7)	68.8 (20.3)
Emotional	81.1 (17.6)	83.7 (17.4)	58.0 (26.2)	62.4 (27.4)
Social	89.1 (13.4)	92.8 (10.9)	73.9 (23.5)	78.0 (24.8)
School	70.7 (19.2)	74.4 (19.5)	54.3 (18.3)	60.2 (23.5)
PedsQL-RM	82.4 (14.1)	83.0 (13.3)	62.4 (18.9)	71.5 (19.5)
Pain and hurt	75.2 (20.3)	75.9 (18.8)	53.5 (26.2)	65.5 (23.5)
Daily activities	93.9 (13.3)	94.3 (11.9)	85.9 (18.4)	89.3 (13.8)
Treatment	87.2 (16.2)	84.5 (14.3)	69.7 (20.2)	76.6 (19.3)
Worry	73.7 (25.7)	75.6 (26.4)	46.4 (28.6)	63.4 (31.5)
Communication	82.1 (21.0)	84.8 (17.9)	56.5 (33.4)	62.7 (34.9)
Functional Disability Index (FDI)	4.7 (5.9)	3.4 (4.7)	8.7 (6.9)	6.5 (5.8)

Table 5

Demographics of Low Risk vs High Risk Groups

Measures	Low Risk Group n=27		High Risk Group n=23		p-value
Patient Factors					
Age (Years)	15.5 (2.4)		17.0 (2.5)		0.04 [‡]
Female		19 (70%)	23 (100%)		N/A
Race					
African American		14 (52%)	9 (40%)		N/S*
Caucasian		11 (41%)	12 (52%)		N/S*
Other		2 (7%)	2 (8%)		N/S*
Disease Duration (Years)	2.3 (2.3)		3.2 (3.0)		0.25 [‡]
Parent Factors					
Parent education level					
High School Diploma		6 (22.2%)	8 (34.7%)		
Some college, trade, vocational		13 (48.1%)	7 (30.4%)		
Bachelors or 4 year degree		4 (14.8%)	2 (8.7%)		
Masters or Professional		2 (7.4%)	3 (13%)		
Missing		2 (7.4%)	3 (13%)		
Annual Parent Income (in USD)					
<25k		7 (25.9%)	4 (17.4%)		
25k-50k		8 (29.6%)	7 (30.4%)		
50k-75k		3 (11.1%)	-		
75k-100k		1 (3.7%)	3 (13.0%)		
>100k		4 (14.8%)	4 (17.4%)		
Missing		4 (14.8%)	5 (21.7%)		
Insurance					
Public		10 (37%)	8 (34.8%)		
Private		15 (55.6%)	11 (47.8%)		
Missing		2 (7.4%)	4 (17.4%)		

₇ Denotes use of Students T-test to determine p-values comparing means at visit 1 and 2

* Denotes use of chi-square test for categorical variables at visit 1 and 2

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