Functional status in severe juvenile idiopathic arthritis in the biologic treatment era: an assessment in a French paediatric rheumatology referral centre

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Abstract

Objectives. To investigate the functional status of difficult-to-treat JIA patients, including patients receiving biotherapies, and to correlate functional status to disease activity.

Methods. All JIA patients consecutively evaluated in a paediatric rheumatology referral centre (November 2008 to March 2009) were enrolled in an observational cross-sectional study. The Childhood HAQ (CHAQ), physician’s assessment of overall disease activity, parent’s assessment of well-being and pain, and active and limited joint numbers were measured.

Results. We enrolled 95 patients [27% systemic, 29% polyarticular, 22% enthesitis-related arthritis (ERA) and 23% oligoarticular JIA]. Median disease duration was 3.5 years. Treatment included NSAIDs (56%), MTX (23%), CSs (21%) and biologics (45%). Of all patients, 31 and 56%, respectively, had inactive and minimally active disease. The median CHAQ score was 0.375 (range 0–3). Most patients had no or mild functional disability (61%), impaired well-being (63%) or pain (55%); 10% reported severely impaired function and well-being, 19% severe pain. ERA patients reported worse well-being and pain. CHAQ scores correlated with disease activity. Long-lasting disease and biologic treatment were associated with better well-being and pain scores.

Conclusion. Despite the high proportion of severe JIA patients in this cohort, CHAQ values are within the lower range of recent reports, probably related to new therapeutic approaches. Impaired function and well-being remain a challenge for at least 10% of the patients. Impaired well-being and pain in ERA patients require further study. The strong correlation between functional status and well-being underlines the importance of improving function to optimize quality of life.

Key words: juvenile idiopathic arthritis, outcome measures, disease activity, biologic treatment.

Introduction

The functional outcome of patients with JIA is an important issue in the field of paediatric rheumatology. Recent literature shows a marked reduction in the proportion of patients experiencing serious long-term functional impairment [1–4]. In the past decade, the treatment of JIA has advanced significantly thanks to the widespread use of MTX and IA CSs, the early introduction of second-line medication and, in recent years, the availability of biologic response modifiers. When applied early in the disease process, these new approaches are expected to lead to improved short- and long-term outcome of JIA patients [5–12].

In the present study we aimed to address the impact of recent therapeutic progress by evaluating the current functional status of a group of JIA patients referred to a tertiary care paediatric rheumatology centre. In this observational cross-sectional study, we particularly focused on the relation between functional status and parameters of disease activity. We also assessed possible differences in
functional status of patients with different JIA subtypes and differences between JIA patients receiving biologic treatment and those receiving standard treatment.

Patients and methods

Patients

Between November 2008 and March 2009, all JIA patients evaluated at the French National Reference Center for Juvenile Arthritis at Hôpital Necker-Enfants Malades, Paris, France, were enrolled in this study. The inclusion criteria were the diagnosis of JIA according to the ILAR criteria [13] and the age of ≤18 years at the time of evaluation. Patients’ and parents’ information, data collection and analysis were conducted in accordance with French National Guidelines. Patients were recruited through the Centre de référence des Maladies Rares (CEMARA) database system following approval of the French Commission Nationale Informatique et Liberté and informed consent.

Clinical assessment

At the study visit, patient and disease characteristics were recorded: gender, age at disease onset, age at diagnosis, age at study visit, JIA subtype, presence of ANAs, history of uveitis and current therapy. The paediatric rheumatologist documented the physician’s assessment of overall disease activity on a 10-cm visual analogue scale (VAS) (VAS physician), the number of active joints (defined as the number of joints with swelling or, if no swelling was present, with limitation of movement and pain upon movement or tenderness) and the number of joints with limitation of motion (LOM). The articular indices were assessed in a total of 73 joints. The patient’s parent provided an assessment of the child’s overall well-being and pain, both on a 10-cm VAS (VAS well-being and VAS pain, respectively), and completed the French version of the Childhood HAQ (CHAQ). For the purpose of analysis, all VAS scores were converted to a 0–3 score by multiplying each VAS value by a factor of 0.03. Next, the CHAQ and VAS well-being and pain scores were divided into four categories of severity: score = 0 (none), 0 < score ≤ 0.5 (mild), 0.5 < score ≤ 1.5 (moderate) and score > 1.5 (severe), as previously described [14].

Clinically inactive disease

Clinically inactive disease was defined as an active joint count of zero and a VAS physician indicating no disease activity, absence of systemic manifestations attributable to JIA and absence of active uveitis regardless of whether the patient was receiving medical treatment. For patients with enthesitis-related arthritis (ERA), absence of enthesitis was an additional criterion. Although ESR and CRP values are included in the definition of clinical remission according to Wallace et al. [15], they were not systematically recorded here, as this was a cross-sectional survey in a centre where blood sampling is not performed at each visit.

Minimal disease activity

Minimal disease activity was defined as follows. For oligoarthritis (i.e. patients with the ILAR category of persistent oligoarthritis or ERA with an oligoarticular course): a VAS physician of ≤ 2.5 cm and an active joint count of zero; for polyarthritis [i.e. patients with ILAR categories of extended oligoarthritis, polyarthritis, ERA or systemic JIA (SJIA) with polyarticular course]: a VAS physician of ≤ 3.4 cm, a parent’s VAS well-being ≤ 2.1 cm and an active joint count ≤ 1 [16]. Of note, uveitis was not taken into account, as it was not proposed in the definition of minimal disease activity. For SJIA we added the requirement of no systemic manifestations attributable to JIA. Finally, for ERA, the absence of enthesitis was an additional criterion. A special focus was made on differences in functional status, well-being and pain of patients with different JIA subtypes.

For the purpose of analysis, in the current study the patients were divided in three groups according to disease duration: duration <2 years (early disease), duration 2–6 years (intermediate disease) and duration >6 years (long-lasting disease). In addition, patients with extended oligoarthritis were grouped and analysed together with RF-negative polyarthritis patients.

Statistical analysis

Comparisons between groups of patients were performed using the Mann-Whitney U-test for testing of two groups, and the Kruskal-Wallis test for testing of more than two groups, with the Dunn’s test as an a posteriori test for pair-wise comparisons. Correlation was tested using the Spearman’s rank correlation test. P-values < 0.05 were considered as evidence for statistical significance.

Results

Patient population

A total of 95 JIA patients was included. The demographics, general disease characteristics, clinical features and treatment are shown in Table 1. All JIA subtypes were represented. A female predominance was seen in all JIA subtypes except for the SJIA and ERA subgroups. Eighty-eight per cent of patients (84/95) received systemic medical treatment. For the patients who were on systemic CSs, the mean daily dose was 0.3 ± 0.2 mg/kg/day. Among 45% of patients (43/95) receiving biologic treatment, 18 had SJIA, 7 RF-negative polyarthritis, 6 extended oligoarthritis, 5 oligoarthritis, 5 RF-positive polyarthritis and 2 ERA. Fourteen per cent of patients (13/95) received a combination of biologics (etanercept, adalimumab, abatacept) and MTX. Among 14% of patients (13/95) with a history of uveitis (Table 1), five still had active uveitis.

Disease activity

The median values for the parameters of disease activity are given in Table 1. Overall, 54% of patients (51/95) had zero active joint count; 63% (60/95) had ≤ 1 cm VAS physician and 37% (35/95) had 0 cm VAS physician. Thirty-one per cent of patients (29/95) met the criteria
for inactive disease, including 36% (8/22) oligoarthritis, 33% (2/6) extended oligoarthritis, 33% (5/15) RF-negative polyarthritis, 17% (1/6) RF-positive polyarthritis, 24% (6/25) SJIA and 29% (6/21) ERA patients. Moreover, 56% of patients (53/95) fulfilled the criteria for minimal disease activity, including 55% (12/22) oligoarthritis, 67% (4/6) extended oligoarthritis, 53% (8/15) RF-negative polyarthritis, 50% (3/6) RF-positive polyarthritis, 60% (15/25) SJIA and 43% (9/21) ERA patients. Among them, 9% (5/53) had active uveitis (3 oligoarthritis, 1 extended oligoarthritis and 1 RF-negative polyarthritis patients).

Function, well-being and pain
Sixty-one per cent of the patients (57/95) reported no or mild functional disability. However, 10% reported severe impairment (9/95): 5 patients with SJIA, 2 RF-positive polyarthritis and 2 ERA patients. These patients were older at disease onset compared with the other 86 patients [median 8 years (range 0.5–11.5 years) vs 4 years (range 0.5–15 years)]. They had active disease when functional assessment was performed. Also, four of them had particularly severe and difficult-to-control disease as assessed by the fact that they had received more than two biologics.

Of all CHAQ categories, those most affected were activities, dressing and reaching. Almost two-thirds of the patients (60/95, 63%) mentioned either no or mild impact of their disease on overall well-being, whereas 8% (8/95) reported severe impact. Conversely, whereas 55% (52/95) also reported no or mild pain, 19% (18/95) reported severe pain (Fig. 1A).

Function, well-being and pain according to JIA subtype
In a subgroup analysis we tested the patients according to JIA subtype, first, for differences in disease activity parameters (Table 2) and, secondly, for differences in the categorical severity scores for function, well-being and pain (Fig. 1B–E).

Table 2 shows that the active joint number and the VAS physician scores did not differ between JIA subgroups. The limited joint number was significantly higher in SJIA patients relative to oligoarthritis and ERA patients. Overall, functional ability as assessed by CHAQ was most impaired in ERA patients, followed by RF-positive and RF-negative polyarthritis, and then by SJIA and oligoarthritis; however, these differences did not reach statistical significance. VAS well-being was highest for ERA patients, followed by SJIA, RF-positive polyarthritis and RF-negative polyarthritis, and oligoarthritis; this difference was significant only for ERA patients relative to oligoarthritis patients. VAS pain was significantly higher in ERA vs
**Fig. 1** Distribution of all JIA patients (A) and JIA subtype patients (B–E) according to different categories of severity for CHAQ scores (range 0–3, *0*, 0.125–0.5, *0.625–1.5, †>1.5) for VAS well-being and for VAS pain scores (range 0–10 cm, *0*, 0.1–1.7, †1.8–5, ‡>5).

**Table 2** CHAQ and parameters of disease activity in the total JIA group and according to JIA subtype

<table>
<thead>
<tr>
<th>Parameter</th>
<th>All patients (n = 95)</th>
<th>Oligoarthritis (n = 22)</th>
<th>Polyarthritis RF– (n = 21)</th>
<th>Polyarthritis RF+ (n = 6)</th>
<th>SJIA (n = 25)</th>
<th>ERA (n = 21)</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of active joints</td>
<td>0 (0–28)</td>
<td>0 (0–4)</td>
<td>0 (0–17)</td>
<td>6 (0–26)</td>
<td>0 (0–28)</td>
<td>1 (0–11)</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Number of joints with LOM</td>
<td>1 (0–45)</td>
<td>0 (0–5)</td>
<td>2 (0–45)</td>
<td>4 (0–26)</td>
<td>2 (0–37)</td>
<td>0 (0–11)</td>
<td>0.001*</td>
</tr>
<tr>
<td>VAS physician*</td>
<td>0.7 (0–7.0)</td>
<td>0 (0–2.0)</td>
<td>0.3 (0–5.7)</td>
<td>0.9 (0–4.0)</td>
<td>1.3 (0–7.0)</td>
<td>1.1 (0–6.0)</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>VAS pain†</td>
<td>0.9 (0–9.7)</td>
<td>0.3 (0–6.0)</td>
<td>0.5 (0–5.1)</td>
<td>0.8 (0–3.7)</td>
<td>0.9 (0–6.8)</td>
<td>2.0 (0–9.7)</td>
<td>0.042**</td>
</tr>
<tr>
<td>VAS well-being‡</td>
<td>1.0 (0–8.7)</td>
<td>1 (0–8.0)</td>
<td>0.4 (0–6.4)</td>
<td>0.3 (0–1.0)</td>
<td>0.7 (0–7.0)</td>
<td>4.4 (0–8.7)</td>
<td>0.002***</td>
</tr>
<tr>
<td>CHAQ§</td>
<td>0.375 (0–3)</td>
<td>0.125 (0–1.375)</td>
<td>0.250 (0–1.125)</td>
<td>0.250 (0–2.375)</td>
<td>0.125 (0–3)</td>
<td>0.500 (0–2.375)</td>
<td>&gt;0.05</td>
</tr>
</tbody>
</table>

Results are expressed as median (range). *Kruskal–Wallis test; †VAS scale 0–10 cm; ‡CHAQ scale 0–3. *SJIA vs ERA (P = 0.005), SJIA vs oligoarthritis (P = 0.006) (Dunn’s test); **ERA vs oligoarthritis (P = 0.046) (Dunn’s test); ***ERA vs oligoarthritis (P = 0.043), ERA vs SJIA (P = 0.016), ERA vs RF-negative polyarthritis (P = 0.015), ERA vs RF-positive polyarthritis (P = 0.039) (Dunn’s test).
Fig. 1B–E shows the classification within JIA subtypes according to categories of function, well-being, and pain. More than two-thirds of oligoarthritis and polyarthritis patients reported no or mild impairment of function (68%, respectively, 67%) and no or mild impairment of well-being (77%, respectively, 70%). Similarly, 54% of oligoarthritis and 65% polyarthritis patients reported no or mild pain; conversely, severe pain was reported by 23% of oligoarthritis patients as compared with only 5% of polyarthritis patients (Fig. 1B–C). More than half (56%) of the SJIA patients reported either no or mild impairment of function and well-being, and 65% experienced no or mild pain (Fig. 1D). On the other hand, about half of ERA patients showed moderate to severe impairment of function and well-being (48% and 52%, respectively), and 43% reported severe pain (Fig. 1E).

Correlations of CHAQ score with disease activity parameters

In order to selectively assess the impact of disease activity on functional status, we correlated CHAQ scores (expressed on standard CHAQ scale 0–3) with five other indices of disease activity. This was tested for the entire JIA patient group and for the JIA subtype subgroups (Table 3). In the overall JIA group, functional disability correlated with all five parameters, the correlation being stronger for VAS well-being and VAS pain. In the analysis according to JIA subtype, the correlation between functional disability and VAS well-being and pain was confirmed for every JIA subtype. Functional disability correlated with the number of active joints in SJIA patients as well as with the number of joints with LOM in both SJIA and polyarthritis patients. Finally, functional disability correlated with the VAS physician in all but oligoarthritis patients.

**Disease duration and parameters of function and disease activity**

In order to relate disease duration with functional status and disease activity, we divided the total JIA patient group into three categories of disease duration (see ‘Patients and methods’ section). First, we sought for possible differences in functional and disease activity scores between these three groups. Table 4 shows that the patients with long-lasting disease showed significantly better scores for well-being and pain. Although they also presented with the best CHAQ and VAS physician scores, differences did not reach significance. There was no significant difference in the numbers of active or limited joints.

Next, we sought a possible correlation between the CHAQ score and the parameters of disease activity in each subgroup of disease duration (Spearman’s rank correlation test, data not shown). The CHAQ score correlated with VAS well-being score, irrespective of disease duration in the numbers of active or limited joints.

TABLE 3 Correlation between CHAQ and disease activity parameters in the total JIA group and in JIA subtype groups

<table>
<thead>
<tr>
<th>Parameter</th>
<th>CHAQ^b</th>
<th>CHAQ^b</th>
<th>CHAQ^b</th>
<th>CHAQ^b</th>
<th>CHAQ^b</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>All (n = 95), r</td>
<td>Oligoarthritis (n = 22), r</td>
<td>Polyarthritis RF (n = 21), r</td>
<td>SJIA (n = 25), r</td>
<td>ERA (n = 21), r</td>
</tr>
<tr>
<td>Number of active joints</td>
<td>0.436*</td>
<td>-0.017</td>
<td>0.152</td>
<td>0.708*</td>
<td>0.234</td>
</tr>
<tr>
<td>Number of joints with LOM</td>
<td>0.237**</td>
<td>-0.026</td>
<td>0.529**</td>
<td>0.499</td>
<td>0.099</td>
</tr>
<tr>
<td>VAS physician’s^c</td>
<td>0.493*</td>
<td>0.222</td>
<td>0.612**</td>
<td>0.666*</td>
<td>0.452***</td>
</tr>
<tr>
<td>VAS well-being^c</td>
<td>0.698*</td>
<td>0.722*</td>
<td>0.601**</td>
<td>0.597**</td>
<td>0.639**</td>
</tr>
<tr>
<td>VAS pain^c</td>
<td>0.633*</td>
<td>0.809*</td>
<td>0.603**</td>
<td>0.468**</td>
<td>0.535**</td>
</tr>
</tbody>
</table>

^aResults are expressed as r, as defined by the Spearman’s rank correlation test; ^bCHAQ scale 0–3; ^cVAS scale 0–10 cm. *P < 0.001, **P < 0.025, ***P < 0.05.

TABLE 4 CHAQ and disease activity parameters according to disease duration in the total JIA patient group

<table>
<thead>
<tr>
<th>Parameter</th>
<th>&lt; 2 years (n = 27)</th>
<th>2–6 years (n = 31)</th>
<th>&gt; 6 years (n = 32)</th>
<th>P^a</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of active joints</td>
<td>1 (0–26)</td>
<td>0 (0–28)</td>
<td>0 (0–17)</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Number of joints with LOM</td>
<td>0 (0–16)</td>
<td>2 (0–45)</td>
<td>1 (0–37)</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>VAS physician’s^b</td>
<td>1.0 (0–4.0)</td>
<td>0.6 (0–7.0)</td>
<td>0.5 (0–5.7)</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>VAS well-being^b</td>
<td>1.5 (0–5.1)</td>
<td>1.3 (0–7.0)</td>
<td>0.2 (0–6.5)</td>
<td>0.034*</td>
</tr>
<tr>
<td>VAS pain^c</td>
<td>2.3 (0–8.0)</td>
<td>1.0 (0–8.7)</td>
<td>0.4 (0–7.0)</td>
<td>0.047**</td>
</tr>
<tr>
<td>CHAQ^c</td>
<td>500 (0-2.375)</td>
<td>375 (0-2.375)</td>
<td>0 (0-3)</td>
<td>&gt;0.05</td>
</tr>
</tbody>
</table>

^aResults are expressed as median (range). ^bKruskal–Wallis test; ^cVAS scale 0–10 cm; ^dCHAQ scale 0–3. ^e>6 years vs 2–6 years (P = 0.040), >6 years vs <2 years (P = 0.037) (Dunn’s test); ^f>6 years vs <2 years (P = 0.030) (Dunn’s test).
Data are expressed as median (range). aMann–Whitney U-test; bVAS scale 0–10 cm; cCHAQ scale 0–3.

Table 5 CHAQ and disease activity parameters in the total JIA group with or without biologic treatment

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Biologic treatment (n = 43)</th>
<th>No biologic treatment (n = 52)</th>
<th>P&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of active joints</td>
<td>0 (0–28)</td>
<td>1 (0–16)</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Number of joints with LOM</td>
<td>1 (0–37)</td>
<td>0 (0–45)</td>
<td>0.049</td>
</tr>
<tr>
<td>VAS physician’s score</td>
<td>0.5 (0–5.7)</td>
<td>0.8 (0–7.0)</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>VAS well-being score</td>
<td>0.4 (0–8.7)</td>
<td>1.4 (0–7.0)</td>
<td>0.019</td>
</tr>
<tr>
<td>VAS pain score</td>
<td>0.5 (0–8.0)</td>
<td>2.4 (0–8.7)</td>
<td>0.016</td>
</tr>
<tr>
<td>CHAQ score&lt;sup&gt;c&lt;/sup&gt;</td>
<td>0.125 (0–2.375)</td>
<td>0.375 (0–3)</td>
<td>&gt;0.05</td>
</tr>
</tbody>
</table>

Discussion

With this cross-sectional study on the functional status of a cohort of 95 JIA patients at a paediatric rheumatology referral centre, we aimed to address the impact of recent therapeutic progress on difficult-to-treat JIA. This study mainly included difficult-to-treat patients, as 69% had active disease at assessment and a high percentage had either SJIA or JIA with a severe polyarticular outcome, whereas in prior studies oligoarthritis and polyarthritis were the most represented subtypes [1, 2, 14, 17–24]. The percentage of ERA patients was also higher than in most studies on function in JIA so far [2, 19, 20, 22–26]. Remarkable is the high percentage (45%) of patients receiving biologic treatment, in contrast with recent studies [1, 2, 19, 24], probably as a consequence of many difficult-to-treat JIA patients in our referral centre. Our findings can therefore be considered to reflect the functional status of severe JIA patients in the current era of effective and novel therapies.

Accurate comparison of this study with existing literature on functional status in JIA is hampered by heterogeneity in patient samples (including JIA subtype distribution, disease duration, standard therapy vs biologic treatment) as well as study methodology (clinical assessment and analytical approach). While taking this limitation into account, we cautiously draw the following conclusions.

Overall, our patients had similar or lower active joint numbers and better VAS physician scores than those reported in most previous studies [1, 2, 4, 18–20, 24, 26, 27]. Moreover, the criteria for inactive and minimally active disease were fulfilled by 31 and 56% of patients, respectively, proportions that are similar to or higher than those reported earlier [1, 2, 22, 23, 28]. Thus, in this cohort, despite the high proportion of difficult-to-treat JIA patients, the disease was well controlled.

The median CHAQ score of the present cohort is well within the lower range of those previously reported (0–0.8). Overall, our patients presented with superior functional, well-being and pain scores relative to those in most existing reports [2, 4, 19, 20, 25–27]. Not surprisingly, these scores were worse than the ones described in selected cohorts comprising higher proportions of oligoarthritis patients (31.6–58%) [1, 14, 22]. Importantly, however, severe functional disability (i.e. CHAQ >1.5) was still reported by 10% of our patients, a subgroup that consisted mainly of patients with SJIA, but also patients with RF-positive polyarthritis and ERA. This proportion is clearly higher than those reported in both older and recent studies [1, 14], and indicates that in the current era of new therapies there still is room for improvement.

We found functional ability to be similar among the different JIA subtypes; this is in contrast to previous reports where polyarthritis and SJIA patients showed worse functional status than oligoarthritis patients [14, 17, 22, 27]. This improvement in functional status may be attributed, at least in part, to the use of new therapies.
Interestingly, ERA patients in our cohort reported worse scores for well-being and pain than polyarthritis and SJIA patients, whereas the VAS physician scores were not significantly different. Two recent studies similarly reported inferior well-being and pain evaluations in ERA patients [26, 29]. Specific disease manifestations such as axial involvement and enthesitis may explain this observation. However, the impact of enthesitis on well-being and pain experience is most probably underestimated in this cohort, even in the VAS physician score. On the other hand, neither the CHAQ scores nor the well-being or pain scores were found to be different between ERA patients with documented enthesopathy and those without (data not shown). Since all but two ERA patients received standard therapy, the possible beneficial effect of biologic treatment in this particular subgroup could not be evaluated and this is an important question to be addressed in future studies. An unexpectedly high proportion of polyarthritis patients reported severe pain. Relative to the remainder of oligoarthritis patients, these patients showed similar joint involvement, but shorter disease duration (median 1.5 vs 6 years). This observation might indicate that pain or its perception is increased during the early phase of disease.

As has been described previously, the CHAQ score correlated with well-being and pain scores in the total JIA group, but also within all JIA subtype groups and within all disease duration groups; one exception was the absence of correlation with pain in patients with early disease [2, 14, 18]. These findings reveal once more the strong relation between function, well-being and pain.

We documented better scores for CHAQ, well-being and pain in patients with longer disease duration, and this confirms the evolution towards improvement of functional outcome reported in previous literature [3, 4, 18, 19, 26, 28, 30]. However, few reports on JIA patients treated during the previous decades have shown the worst functional impairment in patients with longer disease [14, 31]. Our findings therefore endorse the major impact of newer therapeutic approaches on disease outcome.

An intriguing feature was that patients receiving biologic treatment (mostly patients with polyarthritis and SJIA) had more joints with LOM but better functional ability, well-being and pain scores compared with the other patients. Although the severity of LOM was not recorded in our study, most patients had SJIA or polyarthritis with severe and multiple large and small joint involvement. Better control of functional impairment and pain may reflect better control of disease activity in patients on biologics. It is also plausible to expect that dramatic improvement in disease activity, as a consequence of efficient therapy, positively influences the subjective appreciation of well-being and pain. Pain is an important factor influencing functional ability, and our patients reporting better functional abilities had lower pain scores. Overall, these findings underscore the potential of novel therapies not only to control active inflammatory disease, but equally to improve the functional status and quality of life of patients with severe JIA.

This study is confronted with some limitations. As mentioned, the study sample consisted of all patients consecutively receiving care at a paediatric rheumatology referral centre, leading to an over-representation of patients with severe disease. This allows for an estimation of the impact of modern therapeutic approaches on the outcome of patients with severe and difficult-to-treat JIA, but limits the generalization of our findings to the overall JIA population. Evaluation of disease severity did not include the evaluation of joint destruction, and it will be of interest to take this into account in future studies. The numbers of patients for each JIA subset were small; however, similar numbers of patients in each of the four main subgroups (SJIA, oligoarthritis, RF-negative polyarthritis and ERA) facilitated comparative statistics. Relative to an overall JIA population, the ERA subgroup was over-represented, and this permitted the specific evaluation of this JIA subtype. On the other hand, classical measures of JIA disease activity used in this study have not been validated in this subgroup, and in future studies it would be appropriate to include more specific assessment tools for ERA, such as the BASDAI score. The impact of uveitis on outcome in JIA patients in our study was not thoroughly assessed. Unfortunately, many actual measures of disease activity do not specifically take uveitis into account, and in this context, the development of more complex JIA assessment tools considering uveitis would be of great interest.

In conclusion, new therapeutic approaches including biologics may explain the limited functional impairment—as assessed by the CHAQ score—observed in the current study cohort in which difficult-to-treat JIA patients are over-represented. Nevertheless, achieving optimal functional status remains a challenge for a significant proportion of these patients. In particular, studies focusing on functional status in ERA will benefit the outcome in these patients. A continued research focus on functional status in JIA through studies using assessment tools appropriate for each JIA subtype will allow for further improvement of the long-term functional outcome in JIA and the determinants of well-being and quality of life.

**Rheumatology key messages**

- Limited functional impairment in difficult-to-treat JIA patients is probably related to new therapeutic approaches including biologics.
- Achieving optimal functional status remains a challenge for a significant proportion of JIA patients.

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References


