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Original article

Impaired quality of life after chikungunya virus infection: a 2-year follow-up study

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Abstract

Objectives. To measure the frequency of and risk factors for rheumatic manifestations after chikungunya virus (CHIKV) infection and to assess their impact on quality of life (QoL).

Methods. In a cohort study among 509 cases diagnosed in France, demographic and clinical characteristics were collected at baseline, and QoL status by 36-item short-form health survey (SF-36), a short form of the Arthritis Impact Measurement Scales 2 (AIMS2-SF) and General Health Questionnaire (GHQ-12) at follow-up. SF-36 scores were compared with population norms. Factors associated with QoL were identified in multivariate linear regression models.

Results. A total of 391 (77%) patients participated (53.5% female, mean age 50.2 years). Median time from onset at follow-up was 23.4 months. Among 176 recovered patients, a shorter duration of symptoms was observed in younger age groups and male patients. The probability of full recovery at 1 year was 0.39. Those not recovered were older, had more comorbidities and a longer acute stage with joint swelling. Scores of physical and mental components of the SF-36 and GHQ-12 were low. The AIMS2-SF was affected mainly in symptoms, psychological and social dimensions. Recovered patients did not differ significantly from age- and gender-matched population SF-36 norms. Older age ($P = 0.01$–0.002) was associated with lower SF-36 scores. Other factors associated with lower SF-36, lower GHQ12 scores and higher AIMS2-SF dimensions were lack of recovery ($P = 0.017$ to <0.0001), presence of comorbidity ($P = 0.005$ to <0.0001) and a longer duration of acute stage ($P = 0.047$ to <0.0001).

Conclusion. Medical follow-up with special attention to comorbidity providing information on possible chronic symptoms and giving support for potential depression and anxiety are recommended.

Key words: chikungunya infection, quality of life, France.

Introduction

Chikungunya virus (CHIKV) infection is caused by an arboviral alphavirus transmitted to humans by *Aedes* mosquitoes. In 2005, an outbreak of CHIKV infection occurred on the islands of the Indian Ocean. On Reunion Island, 38.2% of the 785 000 inhabitants were infected between March 2005 and September 2006 [1] and several hundreds of cases were consequently reported in mainland France among returning travellers [2]. Seventy per cent of these cases were reported not to be cured 4 months after onset of CHIKV infection [3]. Rheumatic manifestations persisting several months or years after acute infection have been previously reported [4–8]. The persistence of symptoms without any tool to predict either healing or clinical relapses may be associated with severe distress and affect health-related quality of life (QoL). In 2009, a study among residents of Reunion Island suggested that some dimensions of QoL might still be affected after an average of 17 months [6].

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The impact of rheumatic diseases on QoL has been studied for rheumatic diseases like OA, RA and AS, using generic and disease-specific self-report questionnaires [9–10]. Generic instruments allow comparison with norms issued from the general population when available. Arthritis-specific instruments are acceptable for post-CHIKV rheumatism whose symptoms, mode of evolution and unpredictable duration are close to those of inflammatory arthritis. To measure the frequency of and risk factors for rheumatic manifestations after CHIKV infection and to assess their long-term impact on QoL, we conducted a cohort study among imported cases diagnosed in mainland France from March 2005 to 2007.

Methods

In 2005, a laboratory-based surveillance system of imported cases of CHIKV infection was set up in mainland France to allow the detection and management of cases in areas with the potential vector *Aedes albopictus* to prevent transmission [11]. Persons eligible for the study were identified through this surveillance system [2].

A patient was a person with clinical symptoms of CHIKV infection confirmed by the presence of CHIKV-specific IgM antibody or detection of CHIKV using RT-PCR from March 2005 to 2007. The patients' postal addresses and telephone numbers were obtained by their microbiologists or physicians after oral consent. In mid-December 2007, a self-administered standardized questionnaire was mailed to 509 patients with a known address. The study was approved by the Comité Consultatif sur le traitement de l'information en matière de recherche dans le domaine de la santé and by the Commission nationale de l'informatique et des libertés.

Data were collected on demographic characteristics and clinical manifestations of CHIKV infection: during the acute stage, from the acute stage to time of assessment and in the previous week. Acute stage was defined as the presence of arthralgia and fever lasting for <30 days after symptom onset. Relapse was defined as the reappearance of arthralgia after a substantial decrease in intensity or after a symptom-free period of at least 1 week.

Current health status in terms of generic and specific QoL, mental health and comorbidity were determined using the following:

The 36-item short-form health survey (SF-36) questionnaire [12] is a generic health status questionnaire. It includes eight dimensions scored from 0 (worst) to 100 (best QoL). SF-36 physical and mental components are two weighted combinations of its eight dimensions with physical functioning, role limitations due to physical health problems and bodily pain dominant in the physical component, and mental health, role limitations due to emotional problems and social functioning dominant in the mental component.

The short form of the the Arthritis Impact Measurement Scales 2 (AIMS2-SF) [13] is a specific measure of health status developed and validated for rheumatic diseases, including five dimensions from 0 (best) to 10 (worse QoL).

The General Health Questionnaire (GHQ-12) [14] is a measure of mental health and psychological distress with 12 items rated in four modalities (0–3). It results in one unique score from 0 (worst) to 100 (best psychological health).

The Functional Comorbidity Index (FCI) [15] has been developed to include all comorbidities associated with deterioration of physical QoL. It is scored from 0 to 7 and allows counting the number of comorbidities.

Statistical analyses

The association between recovery and explanatory variables was calculated by relative risk (RR) and 95% CI (univariate analysis). We conducted a multivariate survival analysis for interval-censored data using a backward procedure to estimate the time to full recovery depending on explanatory variables selected with a $P < 0.1$ in the univariate analysis. A survival curve was built using the iterative Turnbull's procedure [16] to study the recovery onset over time. Data used were date of the filling of the questionnaire, date of symptom onset (month/year) and duration of the disease among 15 defined time intervals ($<$15 days, 15 days–1 month, 1–3 months, 3–6 months, 6–9 months, 9–12 months, 12–15 months, 15–18 months, 18–21 months, 21–24 months, 24–27 months, 27–30 months, 30–33 months, $>$33 months, no joint pain). For patients reporting recovery, the lower and upper bounds of their time interval were finite. For patients reporting they had not recovered, the upper bound of their time interval was infinite because the event of interest had not yet occurred at the end of the study period. In the multivariate analysis, a method taking into account time intervals was performed [17, 18] and a Weibull distribution was chosen. Four age groups were used ($<$30, 30–49, 50–69 and $>$69 years). Stata 9 software (StataCorp, TX, USA) and R software (version 2.8.1, R Development Core Team, 2008) were used for statistical analysis.

For the QoL part of the study, quantitative and qualitative variables were described using mean (S.D.) and percentages, respectively. QoL scores were presented by dimension. Data from a French national survey conducted with a random sample population of 35 000 persons [19] were used as reference values for SF-36. SF-36 dimensions were compared with the general population sample-matched for age and gender categories. QoL scores were presented according to the change in health status since disease onset. Patients QoL scores in those who have recovered and not recovered were compared using Student's *t*-test and χ^2-test, respectively. The association of QoL score with comorbidity and with the presence of rheumatic diseases like OA and osteoporosis was analysed by Spearman's correlation coefficient and Student's *t*-test, respectively. QoL levels were studied according to disease duration, duration of acute stage and residual symptoms in the past 7 days.

In multivariate linear regression models, factors associated with QoL at follow-up in univariate analysis

included age at disease onset, disease duration, duration of acute stage, comorbidity score, presence of other rheumatic diseases and current residual symptoms were studied. Statistical significance was set at 0.05 and analyses were run using SAS 9.1.

Results

Seven hundred and fourteen patients with a CHIKV infection diagnosed from March 2005 to 2007 were eligible in the laboratory-based surveillance system. Postal addresses were available for 509 (71%) patients. The overall participation rate was 77% (391/509).

Two-hundred and nine (53.5%) patients were females. The mean age at CHIKV infection onset was 50.2 years (median 52 years; range 6–82 years) and did not differ between men and women (49.6 *vs* 50.9). The age distribution was <30 years 10% ($n = 40$), 30–49 years 32% ($n = 126$), 50–69 years 49% ($n = 190$) and ⩾70 years 9% ($n = 35$).

During the acute stage, 96% (360/376) reported fever, 99% (383/389) arthralgia, 93% (350/377) joint stiffness and 74% (276/373) joint swelling. Small joints of the hands, ankles and feet were most often affected. The duration of the acute stage was <8 days for 50% (171/343) and 8–30 days for 50% (172/343). At the time of assessment, the mean time since onset was 22.9 months (median 23.4 months; range 11.8–40 months). The distribution of the 391 patients by 6-month period since onset of symptoms was none (0–6 months), 1 (6–12 months), 45 (12–18 months), 198 (18–24 months), 129 (24–29 months) and 18 (⩾30 months).

The presence of comorbidity was reported by 60% (227/377) patients, most often degenerative disc disease (52%), arthritis (34%) and depression (23%) (Table 1). They reported, on average, one comorbidity with an FCI score of 1.1 (±1.4). A comorbidity was reported for 62.5% (125/200) of women and 57.6% (102/177) of men ($P = 0.33$). Patients reporting a comorbidity were significantly older at disease onset than those not reporting (mean age 54.2 *vs* 44.7, $P < 10^{-3}$).

Overall, 176 (45%) patients considered themselves recovered and 103 (26%) did not know if they had recovered. The latter did not differ from the 112 patients having not recovered regarding gender, age, comorbidity at time of assessment, delay between onset of symptoms and assessment, duration of the acute stage, presence of fever, arthralgia, stiff or swollen joints during the acute stage or in the previous 7 days and relapses during the studied period. They were therefore included in the analysis as patients not having recovered. Consequently, 215 (55%) patients were considered as not recovered at the time of assessment.

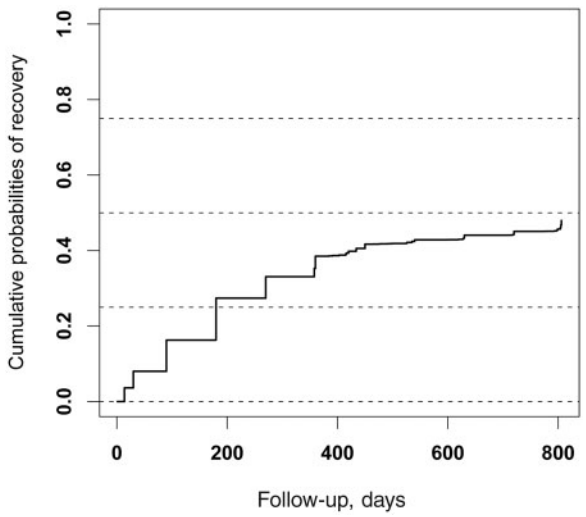
The duration of symptoms was known for 338 (86%) patients. The median interval of the duration of symptoms was 6–9 months (range <15 days to >33 months). The distribution of symptom duration of the 338 patients by 3-month period was 76 (0–3 months), 53 (3–6 months), 30 (6–9 months), 28 (9–12 months), 21 (12–15 months), 12 (15–18 months), 14 (18–21 months), 49 (21–24 months), 36 (24–27 months), 7 (27–30 months) and 12 (⩾30 months). Among recovered patients, those with a duration of symptoms ⩽3 months were more likely to be men, younger than patients with a duration of symptoms >3 months, respectively, 63% (40/63) *vs* 41% (45/110) ($P = 0.004$) and 45.1 *vs* 49.7 years ($P = 0.07$). Those with a duration of symptoms >3 months more often had swollen joints during the acute stage [79% (81/103) *vs* 52% (32/61), $P < 10^{-3}$] and reported relapses more often [73% (49/67) *vs* 45% (46/102), $P < 10^{-3}$]. The probability for full recovery at 1 year was 0.39 (Fig. 1).

Relapses of arthralgia were reported for 72% (274/381) patients. The number of relapses was documented for

Table 1 Self-reported comorbidity at time of assessment, CHIKV infection and QoL study, France

Comorbidity	Proportion of patients ($n = 227$), *n* (%)
RA and OA	78 (34)
Osteoporosis	19 (8)
Asthma	31 (14)
Chronic obstructive pulmonary disease, acquired respiratory distress syndrome or emphysema	21 (9)
Angina	5 (2)
Congestive heart failure (or heart disease)	9 (4)
Heart attack (myocardial infarct)	7 (3)
Neurological disease	0 (0)
Stroke or transient ischaemic attack	5 (2)
Peripheral vascular disease	6 (3)
Diabetes type I or II	23 (10)
Upper gastrointestinal disease (ulcer, hernia, reflux)	24 (11)
Depression	52 (23)
Anxiety or panic disorders	42 (18)
Visual impairment (such as cataract, glaucoma, macular degeneration)	34 (15)
Hearing impairment (very hard of hearing, even with hearing aids)	13 (6)
Degenerative disc disease (back disease, spinal stenosis or severe chronic pain)	118 (52)

Fig. 1 Cumulative probability of patients reporting recovery (Turnbull's method), CHIKV infection and QoL study, France.



88 patients. The mean number of relapses was 4 [median 2 (1–20)] and the mean delay between two relapses was 8 weeks [median 4 weeks (1–99 weeks)]. The intensity of arthralgia decreased with time for 43% (107/251), was variable over time for 41% (103/251), was identical for 18% (46/251) and increased for 8% (20/251). During relapses, the pain returned in the same locations for most patients (97%, 257/265); the other symptoms were morning stiffness for 88% (221/251), swollen joints for 58% (121/208) and fever for 26% (45/171). Relapses were reported more often by patients with a comorbidity [RR 1.19 (1.04, 1.37)], stiff joints [RR 2.01 (1.23, 3.31)] or swollen joints [RR 1.29 (1.08, 1.55)] during the acute stage and with a duration of symptoms >3 months [RR 1.57 (1.31, 1.88)].

Recovery was less frequent among patients >50 years [RR 0.73 (0.59, 0.91)], with comorbidity [RR 0.71 (0.57, 0.88)], with arthritis [RR 0.67 (0.45, 0.98)] and with a longer acute stage [RR 0.61 (0.44, 0.83)] (Table 2). Age, duration of the acute stage and presence of swollen joints at the acute stage were included in the multivariate model. Comorbidity variables statistically significant in the univariate analysis were not included because they were collected at the time of assessment.

In the multivariate analysis, the probability of recovery was lower in the 30- to 49-year age group [hazard ratio (HR) = 0.51 (0.32–0.83)] and in the 50- to 69-year age group [HR = 0.37 (0.23–0.59)] than in the <30-year age group. The duration of the symptoms increased by 49 and 63%, respectively, in those two age groups. Having a duration of the acute stage longer than 15 days increased the duration of the symptoms by 49% and decreased the probability of recovery [HR = 0.51 (0.35–0.76)].

The QoL scores at follow-up were severely affected whatever the instrument used (Table 3). The SF-36 showed low scores in some dimensions, ranging from 75.8 in physical functioning down to 49.0 in vitality. Physical and mental components were low at 46.1 and 43.4, respectively. The AIMS2-SF was also affected (higher scores) mainly in symptoms and psychological and social dimensions, and the GHQ-12 showed a decreased score at 61.7. At the time of assessment, 176 recovered patients had a QoL significantly higher than the 215 not recovered ($P < 0.001$), but 25% of them still had a lower QoL. In recovered patients (87 females and 84 males), there were no significant differences of SF-36 scores compared with the general age- and gender-matched population of 1956 women and 1661 men. An exception of better bodily pain in both genders ($P = 0.03$ and 0.02), better physical functioning in women ($P < 0.001$) and lower emotional role in men ($P = 0.044$) was observed (Table 4). For the 215 non-recovered patients, there was a large decrease of about 20 points in physical and mental functioning ($P < 0.001$) and of about 10 points in social domains, particularly in younger (aged 45–54 years) patients.

There were significant correlations ($P < 0.0001$) of FCI with all dimensions of SF-36 ($\rho = -0.28$ to -0.37), AIMS2-SF ($\rho = 0.22$–0.35) and GHQ-12 ($\rho = -0.24$). The 78 patients reporting OA had a lower QoL by 0.6–1.9 points per dimension of AIMS2-SF and by 6–17 points of SF-36. Mental health by GHQ12 did not differ significantly. Patients with osteoporosis ($n = 19$) did not differ significantly from those without osteoporosis. The duration of the CHIKV infection was significantly correlated ($P < 0.0001$) with all dimensions of SF-36 ($\rho = -0.21$ to -0.47), AIMS2-SF ($\rho = 0.09$–0.43) and GHQ-12 ($\rho = -0.23$). A longer duration of the acute stage was associated with a lower SF-36 physical score, mental limitation and general health, with a lower GHQ-12 score and with a higher (worse) AIMS2-SF physical score. Regarding symptoms reported in the 7 days before assessment, swollen joints were statistically associated with all dimensions of all instruments ($P = 0.04$ to <0.001), while other symptoms like pain and joint stiffness were associated with physical dimensions only ($P = 0.034$ to <0.001).

In multivariate linear regression, factors associated with lower (worse) SF-36 QoL scores were older age ($P = 0.01$–0.002), lack of recovery ($P < 0.0001$), presence of comorbidity ($P = 0.005$ to <0.0001) and longer duration of acute stage ($P = 0.01$ to <0.0001). The covariates explained a moderate to large part of the variance in each dimension ($R^2 = 0.15$ and 0.44), and $R^2 = 0.33$ in the physical component and $R^2 = 0.16$ in the mental component. Factors associated with higher (worse) AIMS2-SF scores were lack of recovery ($P = 0.017$ to <0.0001), presence of comorbidity ($P = 0.0002$ to <0.0001) and longer duration of acute stage ($P = 0.047$–0.003) [$R^2 = 0.097$ (social), 0.16 (role), 0.158 (mental), 0.239 (physical) to 0.35 (symptoms)]. Similar factors were determinants of a lower (worse) GHQ12 score ($R^2 = 0.15$).

Discussion

Among imported confirmed cases of CHIKV infection in mainland France, we studied the presence of rheumatic

TABLE 2 Factors associated with reported recovery of the CHIKV infection (univariate analysis), CHIKV infection and QoL study, France

Patient characteristics	Number reporting recovery ($n = 176$)	Proportion reporting recovery, %	RR	*P*-value
Gender				
Male	87	48	Ref	
Female	89	43	0.89 (0.72, 1.11)	0.30
Age, year[a]				
$\leqslant 50$	93	53	Ref	
>50	83	39	0.73 (0.59, 0.91)	0.005
Presence of $\geqslant 1$ co-morbidity[b]				
Yes	89	39	0.71 (0.57, 0.88)	0.002
No	83	55	Ref	
Type of co-morbidity				
Degenerative disc disease[c]				
Yes	40	34	0.75 (0.54, 1.04)	0.08
No	49	45	Ref	
Arthritis[d]				
Yes	23	29	0.67 (0.45, 0.98)	0.03
No	66	44	Ref	
Time since onset, months				
$\leqslant 24$	116	48	Ref	
>24	60	41	0.86 (0.68, 1.09)	0.20
Acute stage				
Duration, days				
$\leqslant 14$	121	51	Ref	
15–30	33	31	0.61 (0.44, 0.83)	0.0006
Fever				
Yes	165	46	1.04 (0.59, 1.85)	0.87
No	7	44	Ref	
Rheumatic symptoms				
Pain				
Yes	172	45	0.90 (0.40, 2.01)	0.80
No	3	50	Ref	
Stiffness				
Yes	152	43	0.78 (0.55, 1.12)	0.22
No	15	56	Ref	
Swelling				
Yes	116	42	0.80 (0.63, 1.01)	0.07
No	51	53	Ref	
Disease duration, months				
$\leqslant 3$	63	83	Ref	
>3	110	42	0.51 (0.43, 0.60)	$<10^{-3}$
Occurrence of relapse				
Yes	97	35	0.51 (0.41, 0.62)	$<10^{-3}$
No	75	70	Ref	

[a]Age at disease onset; [b]at time of assessment; [c]degenerative disc disease (back disease, spinal stenosis or severe chronic pain); [d]arthritis (RA and OA).

manifestations after the acute stage of disease and particularly their impact on QoL. At median 23.4 months from disease onset, 55% of the patients considered themselves not to have recovered from CHIKV infection. Factors associated with a longer disease duration were older age and an acute stage >15 days. Whatever the duration of the disease and the duration of the acute stage, patients with chronic manifestations of CHIKV infection have a deteriorated QoL as assessed by generic (SF-36), mental (GHQ-12) and specific (AIMS2-SF) tools.

Recovered patients seemed to have a QoL equivalent to the general population whatever the duration of the acute stage. Interestingly, age and gender seemed to have little impact on QoL, as opposed to the general population, where it is known to be lower in women and elderly people. One might infer that the impact of CHIKV infection could be more important in men and younger people. However, the high proportion of comorbidities has a marked impact in all explored dimensions.

To our knowledge, this is the first study combining in-depth investigation of generic, mental and specific QoL among a large number of CHIKV-infected patients with a long follow-up period (2 years on average). Moreover, QoL

Table 3 QoL scores using various instruments (AIMS2-SF, GHQ-12, SF-36 questionnaires) among patients, CHIKV infection and QoL study, France

QoL scores	Recovered patients ($n = 176$) Mean (S.D.)	Non-recovered patients ($n = 215$) Mean (S.D.)
AIMS2-SF[a]		
Physical	0.8 (1.1)	1.8 (1.6)
Symptom	1.6 (1.9)	4.3 (2.5)
Affect	2.4 (1.9)	3.6 (2.1)
Social interaction	4.6 (1.8)	5.2 (1.6)
Role	1.0 (2.1)	2.4 (2.5)
GHQ-12[b]		
Global score	67.1 (16.0)	57.4 (19.8)
SF-36[c]		
Physical functioning	86.4 (20.7)	67.1 (27.1)
Role physical	81.0 (33.7)	46.2 (41.5)
Bodily pain	79.5 (23.2)	48.2 (20.8)
Mental health	67.8 (18.7)	55.3 (21.5)
Role emotional	79.1 (36.9)	50.8 (42.4)
Social functioning	81.8 (22.5)	63.1 (25.9)
Vitality	59.4 (18.9)	40.1 (19.2)
General health	71.1 (20.4)	52.2 (22.9)
Physical component summary	51.8 (8.3)	41.2 (10.1)
Mental component summary	47.2 (10.6)	40.1 (11.9)

[a]AIMS2-SF scores from 0 (best) to 10 (worst); [b]GHQ-12 scores; [c]SF-36 scores from 0 (worst) to 100 (best).

Table 4 SF-36 scores[a] among CHIKV-infected patients reporting non-recovery, recovery and age-matched general population, CHIKV infection and QoL study, France

Gender	General population (GP) ($n = 1956$) Mean (S.D.)	Recovered patients (R) ($n = 87$) Mean (S.D.)	Difference (GP − R)	*P*-value (GP − R)	Non-recovered patients (NR) ($n = 118$) Mean (S.D.)	Difference (GP − NR)	*P*-value (GP − NR)
Women							
Physical functioning	72.2 (22.0)	84.8 (21.5)	12.6	<0.001	63.4 (27.6)	−8.8	<0.001
Role physical	79.0 (33.4)	83.7 (30.9)	4.8	0.166	42.4 (40.5)	−36.6	<0.001
Bodily pain	71.2 (24.1)	77.3 (25.9)	6.2	0.032	45.4 (20.0)	−25.7	<0.001
Mental health	66.0 (18.0)	66.2 (20.7)	0.3	0.905	52.9 (21.2)	−13.0	<0.001
Role emotional	79.3 (33.7)	80.7 (36.5)	1.4	0.735	49.4 (40.5)	−29.9	<0.001
Social functioning	79.4 (22.3)	80.6 (24.4)	1.2	0.662	61.2 (26.0)	−18.2	<0.001
Vitality	58.0 (18.4)	58.4 (20.4)	0.4	0.852	39.2 (19.6)	−18.8	<0.001
General health	68.3 (18.7)	70.3 (22.6)	2.0	0.431	52.5 (22.9)	−15.8	<0.001
Men							
Physical functioning	87.1 (19.9)	87.5 (20.3)	0.4	0.866	71.0 (26.1)	−16.0	<0.001
Role physical	83.9 (30.5)	77.4 (36.9)	−6.5	0.118	49.7 (42.6)	−34.1	<0.001
Bodily pain	76.0 (23.0)	81.1 (19.9)	5.2	0.025	51.5 (21.5)	−24.4	<0.001
Mental health	71.4 (16.7)	69.6 (16.2)	−1.8	0.326	58.2 (21.8)	−13.2	<0.001
Role emotional	85.4 (29.9)	76.7 (38.2)	−8.7	0.044	51.6 (44.8)	−33.8	<0.001
Social functioning	84.1 (20.1)	82.2 (20.9)	−1.9	0.431	65.1 (25.8)	−19.0	<0.001
Vitality	62.2 (17.4)	60.2 (17.5)	−2.0	0.299	41.1 (18.9)	−21.2	<0.001
General health	70.1 (18.4)	71.5 (18.5)	1.5	0.480	51.7 (23.0)	−18.4	<0.001

[a]SF-36 scores from 0 (worst) to 100 (best).

scores among CHIKV-infected patients were compared with those of the French general population.

The study has some limitations. First, the questionnaires were self-administered, patients had no medical examination and recovery was self-perceived. Non-recovered patients may have been more likely to participate to the study. Secondly, the comorbidities may have impacted QoL before CHIKV infection occurrence, but this was not measured and the modifying effect of CHIKV infection cannot be quantified. Arthritis being the

main sequelae of CHIKV infection, the significance of such a comorbidity as a risk factor for non-recovery should be interpreted with caution. Thirdly, QoL was measured in a population of travellers who acquired their CHIKV infection outside mainland France and it could be argued that QoL results could have been different if measured among persons living in a CHIKV endemic country.

During the acute stage, fever and rheumatic symptoms of the small joints were reported predominantly in agreement with recent studies [20–22]. Since 2008, four studies reported high percentages of persons with rheumatic symptoms at 15 months or more after acute CHIKV infection (15, 17, 18 and 24 months), respectively, 57, 44, 64 and 59% [5–8]. One study identified age $\geqslant$45 years as a risk factor associated with the persistence of rheumatic symptoms [5]. In our study, older age was also significantly associated with a long duration of symptoms. The proportion of non-recovery in our study (55%) is close to the 57 and 59% of patients experiencing rheumatic manifestations in two studies [5, 8] carried out in populations with similar mean age. Two other studies [6, 7] found non-recovery rates of 44% in a young population (mean age 42 years) and 64% in an older population (mean age 58 years).

In our study, longer duration of the acute stage was also associated with duration of the symptoms. In one study on Reunion Island [23], overall 32% of the CHIKV patients had rheumatic manifestations at 9 months follow-up: 17% if the duration of the acute stage was $\leqslant$14 days and 84% if $>$14 days [RR 4.95 (3.48, 7.05)]. Relapses of joint pain were reported by 72% of the patients, and the presence of comorbidity, joint stiffness and swelling during the acute stage and a longer duration of the disease ($>$3 months) were associated with relapses. The occurrence of relapse in our study is high compared with other studies [5, 7, 23, 24] and might be due to a longer follow-up and to a different definition of relapse.

QoL impairment in CHIKV-infected patients has similar levels as frequent rheumatic diseases like OA [25] or RA [26], illustrating the severity of the long-lasting QoL impact of the disease. A study on Reunion Island having explored QoL using the SF-12 questionnaire only found a decrease in physical but not in mental domains in confirmed CHIKV-infected patients compared with uninfected individuals matched for age, gender and area of residence [6]. These results are consistent with ours for physical domain, but our data revealed a persistent impact on mental health domain in patients diagnosed in mainland France.

Recommendations can be formulated in the light of these findings. Medical follow-up of CHIKV-infected patients until full recovery is important in order to ensure a return to normal perceived health and QoL. Paying attention to comorbidity may help anticipate a potential great deterioration in their QoL. Patients can be informed that return to normal will progressively occur in most cases and could benefit from sharing of information about the possible chronic symptoms and the unpredictable course of the disease. Support should be given for the potential depression and anxiety that these elements of CHIKV infection can provoke.

Rheumatology key messages

- Older age and previous comorbidities predict a worse QoL for chikungunya-infected patients.
- Chikungunya-infected patients should be offered mental health support for potential chronic sequelae.

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References

1 Renault P, Solet JL, Sisssoko D *et al*. A major epidemic of chikungunya virus infection on Reunion Island, France, 2005–2007. Am J Trop Med Hyg 2007;77:72731.

2 Krastinova E, Quatresous I, Tarantola A. Imported cases of chikungunya in metropolitan France: update to June 2006. Euro Surveill 2006;11:E060824.1.

3 Institut de veille sanitaire. Infection à chikungunya : Etude descriptive des cas importés en France métropolitaine, 2005–2006. Saint-Maurice: Institut de veille sanitaire, 2007.

4 Brighton SW, Prozesky OW, de la Harpe AL. Chikungunya virus infection. A retrospective study of 107 cases. S Afr Med J 1983;63:313–5.

5 Sissoko D, Malvy D, Ezzedine K *et al*. Post-epidemic Chikungunya disease on Reunion Island: course of rheumatic manifestations and associated factors over a 15-month period. PLoS Negl Trop Dis 2009;3:e389.

6 Soumahoro MK, Gérardin P, Boëlle PY *et al*. Impact of chikungunya virus infection on health status and quality of life: a retrospective cohort study. PLoS ONE 2009;4: e7800.

7 Borgherini G, Poubeau P, Jossaume A *et al*. Persistent arthralgia associated with chikungunya virus: a study of 88 adult patients on Reunion Island. Clin Infect Dis 2008;47: 469–75.

8 Larrieu S, Ponderoux N, Pistone T *et al*. Factors associated with persistence of arthralgia among chikungunya virus-infected travellers: Report of 42 French cases. J Clin Virol 2010;47:85–8.

9 Kiltz U, van der Heijde D. Health-related quality of life in patients with rheumatoid arthritis and in patients with ankylosing spondylitis. Clin Exp Rheumatol 2009; 27(Suppl. 55):S108–11.

10 Hawker GA. Experiencing painful osteoarthritis: what have we learned from listening? Curr Opin Rheumatol 2009;21: 507–12.

11 Queyriaux B, Armengaux A, Jeannin C *et al*. Chikungunya in Europe. Lancet 2008;371:723–4.

12 McHorney C, Ware JE, Raczek AE. The MOS 36-item short-form health survey (SF-36): II. Psychometric and clinical tests of validity in measuring physical and mental health constructs. Med Care 1993;31: 247–63.

13 Guillemin F, Coste J, Pouchot J *et al*. The AIMS2-SF: a short form of the Arthritis Impact Measurement Scales 2. French Quality of Life in Rheumatology Group. Arthritis Rheum 1997;40:1267–74.

14 Goldgerg DP, Hillier VF. A scaled version of the General Health questionnaire. Psychol Med 1979;9:139–145.

15 Groll DL, To T, Bombardier C *et al*. The development of a comorbidity index with physical function as the outcome. J Clin Epidemiol 2005;58:595–602.

16 Turnbull BW. The empirical distribution function with arbitrarily grouped, censored and truncated data. J R Stat Soc Series B 1976;38:209–95.

17 Lindsey J, Ryan L. Tutorial in biostatistics: methods for interval-censored data. Stat Med 1998;17:219–38.

18 Griffin JT, Fraser C, Gras L *et al*. The effect on treatment comparisons of different measurement frequencies in human immunodeficiency virus observational databases. Am J Epidemiol 2006;163:676–83.

19 Beck F, Guilbert P, Gaitier A, eds. Baromètre Santé 2005. Saint-Denis: Editions Inpes. 2006,597.

20 Staikowsky F, Talarmin F, Grivard P *et al*. Prospective study of chikungunya virus acute infection in the island of La Reunion during the 2005–2006 outbreak. PLoS ONE 2009;4:e7603.

21 Simon F, Parola P, Grandadam M *et al*. Chikungunya infection: an emerging rheumatism among travellers returned from Indian Ocean islands. Report of 47 cases. Medicine 2007;86:123–37.

22 Borgherini G, Poubeau P, Staikowsky F *et al*. Outbreak of chikungunya on Reunion Island: early clinical and laboratory features in 157 adult patients. Clin Infect Dis 2007;44: 1401–7.

23 Girard P, Gaüzère BA. Les douleurs articulaires du chikungunya 9 mois après la fin de la vague épidémique, La Réunion, France (2005–2006). Une enquête de médecine générale. Bull Epidemiol Hebd 2008;38–40:379–4.

24 Staikowsky F, Le Roux K, Schuffenecker I *et al*. Retrospective study of chikungunya disease in Reunion Island hospital staff. Epidemiol Infect 2008;136:196–206.

25 Rat AC, Coste J, Pouchot J *et al*. *OAKH*QOL: a new instrument to measure quality of life in knee and hip osteoarthritis. J Clin Epidem*i*ol 2005;58:47–55.

26 Lempp H, Thornicroft G, Leese M *et al*. Implications of long-term conditions for both mental and physical health: comparison of rheumatoid arthritis and schizophrenia. Qual Life Res 2009;18:699–707.