Impact of impaired morning function on quality of life in rheumatoid arthritis: results of an exploratory patient survey

Aim: A pan-European survey was conducted to assess the impact of impaired morning function on patients with rheumatoid arthritis. **Materials & methods:** Patients aged 18–65 years with rheumatoid arthritis for \geq 6 months and impaired morning function arising from joint stiffness and pain \geq three-times a week were interviewed using a structured questionnaire. Responses were assessed in the total sample and in subgroups defined by severity of morning stiffness. **Results:** Of the 608 respondents, only approximately a third could perform, unimpaired, morning tasks requiring mobility, with impairment increasing with severity of morning stiffness: (p < 0.05). Impaired morning function affected quality of life in 84% of respondents (severe morning stiffness: 98 vs mild: 56%; p < 0.05). Impaired morning function affected the jobs of 74% of the 271 employed respondents (severe morning stiffness: 79 vs mild: 50%; p < 0.05). **Conclusion:** Impaired morning function adversely affects daily activities, quality of life and work, which increases significantly with severity of morning stiffness.

KEYWORDS: morning stiffness = patients = quality of life = rheumatoid arthritis = survey

People with rheumatoid arthritis (RA) commonly describe symptoms of joint pain and stiffness that are particularly severe in the morning [1]. Such morning stiffness may last for an hour or more in 24–49% of patients [2,3]. In the large QUEST-RA database of more than 5000 patients, 69% experienced morning stiffness [2]. The symptom was not restricted to those with poorly controlled disease, as 44% of those patients considered by their Disease Activity Score (DAS28) to be in a state of remission or low disease activity $(DAS28 \le 2.6 \text{ and } 3.2, \text{ respectively})$ experienced morning stiffness [2]. DAS28 is a widely used composite measure of disease activity but does not directly include assessment of morning stiffness. Morning stiffness is not included as part of the core data set for RA clinical trials, mainly because of suboptimal measurement properties [4]. This may have contributed to the decline in use of morning stiffness as an outcome measure in clinical trials in recent years [5]. Although 51% of clinical studies in RA conducted in the 1980s reported morning stiffness as an outcome measure, this dropped to 25% of studies conducted in the 2000s [5]. Likewise, a review of clinical trials that included patient-reported outcomes and were conducted between 2005 and 2007 found that only 27% assessed morning stiffness [6]. A similar situation exists in clinical practice, as shown in audits of patient records conducted in Canada and Ireland

that found fewer than half included assessment of morning stiffness [7,8].

Morning stiffness is of significance to patients. Many factors affect functional ability and contribute to disability, including stiffness in the morning [9]. Although the biomedical model is the predominant paradigm in modern medicine, with decision-making based on objective tests conducted by the health professional, RA is a disease that may be more appropriately treated on the biopsychosocial model, based on information from the patient [10]. In RA, the patient experience may be more indicative of disease state than objective measures such as erythrocyte sedimentation rate and radiographs [10,11]. Indeed, there is close correlation between responses to patient questionnaires and longterm outcomes such as work disability, premature mortality and costs [11].

It has recently been shown that morning stiffness is associated with early retirement from work [12]; such loss of work is known to reduce quality of life [13]. The impaired morning function arising from morning stiffness may make it difficult to carry out activities that are necessary before work can take place. However, such impact of impaired morning function on work, daily living and quality of life has not been formally assessed. To explore patients' perspectives and experiences relating to these issues and to determine if further

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Future

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study is warranted, a survey was conducted among 750 patients in 11 European countries [14]. The findings are reported for patients of working age, classified according to age range, RA disease duration and severity of morning stiffness, to examine the relative impact of these attributes on ability to perform morning activities, on quality of life and on working life.

Materials & methods

After exploratory face-to-face interviews and focus group discussions with patients, a structured questionnaire was developed and translated by medical translators into local languages (checked by back translation by a different translator) [14]. Telephone interviews were conducted in ten European countries (Belgium, Denmark, Finland, France, Italy, The Netherlands, Norway, Spain, Sweden and the UK), with face-to-face interviews conducted in Poland. Respondents included in the survey were recruited in a variety of ways (e.g., via physicians, patient organizations and advertisements); only those respondents aged 18-75 years and reporting a diagnosis of RA for at least 6 months completed the questionnaire.

Patients were asked if they experience impaired morning function as a result of RA, defined as stiffness and pain in the joints (particularly in the hands) first thing in the morning, with the stiffness and pain possibly causing reduced strength, grip and mobility, and difficulty functioning or performing certain tasks. The definition was intentionally broad and without maximum time stated for the duration of impaired morning function, to allow for heterogeneity in manifestations of RA, and to permit an open exploration of the impact of impaired function in the morning. As an exploratory study to examine the impact of impaired morning function and the relative influence of different patient characteristics on functional ability and quality of life, only patients reporting impaired morning function on 3 or more days a week were included.

Patients included in the survey were asked about their ability to carry out normal morning activities: getting out of bed, brushing teeth, getting in the bath or shower, drying their body and hair, dressing and making breakfast. For each task, patients were asked if they were able to carry out the activity as they have always done, find it difficult but cope on their own, find it difficult and need help from someone else, or find it difficult and have to use a device or tool for assistance. To assess the impact of impaired morning function on quality of life, patients were asked to what extent they agreed with a number of statements using a four-point scale of completely disagree (1) to completely agree (4). Respondents in paid employment were asked about any impact of impaired morning function on their working lives.

The analysis was restricted to patients aged 18-65 years so that the impact of impaired morning function on employment status and working life could be explored, without undue confounding by age. Subgroups were defined according to the age range of respondents (18-45, 46-55 and 56-65 years), disease duration (≤ 2 and > 2 years), work status, duration of impaired morning function (≤60 and >60 min) and severity of morning stiffness. Severity of morning stiffness was assessed by patients, on a scale of 0 (no morning stiffness) to 10 (severe morning stiffness). Patients were categorized according to their response: mild (rating of 1-3), moderate (4-7) and severe (8-10) morning stiffness. Work status was categorized as paid employment, not working due to ill health (i.e., on sick leave or retired early from work on health grounds), retired from work, and not working for other reasons (e.g., homemaker, student, unemployed). T test for dependent samples was carried out to compare the significance (95% level) of differences between the subgroups, accounting for overlap between different subgroups.

Results

Respondents

A total of 608 patients aged 18-65 years completed the questionnaire (TABLE 1). As respondents were recruited by a number of different methods, a response rate was not calculated. There were no differences between male and female respondents with regard to mean age, duration of impaired morning function and severity of morning stiffness, although female respondents had a significantly longer duration of RA than males (mean [SD]: 8.50 [9.2] vs 6.75 [8.0] years; p < 0.05) and males were significantly more likely to be in paid employment (56 vs 41%; p < 0.05).

Respondents with recently diagnosed RA (≤ 2 years) were slightly younger than those with RA for >2 years (mean [SD] age: 46.8 [11.4] vs 49.9 [10.4] years; p < 0.05). Respondents in paid work were younger than those not working due to ill health or retired (mean [SD]: 45.6 [10.4] vs 51.7 [9.6] and 58.9

[4.8] years, respectively; p < 0.05) and had RA for less time (mean [SD]: 6.3 [6.9] vs 11.8 [10.4] and 10.5 [11.9] years, respectively; p < 0.05).

Of the 608 respondents aged 18-65 years, fewer than half (45%) were in paid employment; reasons for not working included retired early due to ill health (14%), retired (11%), homemaker (11%), on sick leave (8%), unemployed (5%), student (3%) and other reasons (3%). Employment was significantly (p < 0.05) lower in older respondents (23% in those aged 56-65 years vs 54 and 59% for ages 46-55 and 18-45 years, respectively) and those with RA for more than 2 years (52 vs 41% of those with RA ≤ 2 years). Conversely, retirement due to ill health was significantly (p < 0.05)higher in older respondents (24% in those aged 56-65 years vs 12 and 6% for ages 46-55 and 18-45 years, respectively) and those with RA for more than 2 years (20 vs 3% of those with RA ≤ 2 years).

There was no significant correlation $(R^2 = 0.0708)$ between impaired morning function and severity of morning stiffness (FIGURE 1), suggesting that severe morning stiffness may be experienced by patients, regardless of duration of impaired morning function. However, there was a significant increase in mean (SD) duration of impaired morning function (54.2 [43.6], 77.6 [55.3] and 108.1 [81.7] min, respectively; p < 0.05 for all comparisons) in subgroups of patients categorized by severity of morning stiffness (mild, moderate and severe). Likewise, morning stiffness was rated as significantly more severe (mean [SD] score: 6.6 [1.7]) in those categorized as having prolonged impairment (>1 h) of morning function (mean [SD] duration: 139.7 [58.1] min) than in those with impairment lasting up to an hour (mean [SD] duration 41.5 [19.3] min, severity rated 5.9 [1.7]; p < 0.05).

There was no difference in mean duration of impaired morning function across subgroups defined by age, although severity rating for morning stiffness increased significantly (p < 0.05) from mean (SD) 5.78 (1.7) in the youngest age group (18–45 years) to 6.32 (1.6) and 6.45 (1.9) in the older age groups (46–55 and 56–65 years, respectively). By contrast, duration of impaired morning function increased with RA duration (mean [SD]: 67.3 [50.0] vs 90.2 [67.5] min, in RA ≤2 and >2 years, respectively; p < 0.05) but there was no difference in morning stiffness severity (mean [SD]: 6.2 [1.7] in both subgroups).

Table 1. Demographic and disease characteristics of r	espondents.
Characteristic	
Total (n)	608
Females (n [%])	453 (74.5)
Mean age (years [SD])	48.9 (10.9)
Age range (n [%])	
18–45 years	197 (32.4)
46–55 years	193 (31.7)
56–65 years	218 (35.9)
Mean RA duration (years [SD])	8.1 (8.9)
RA duration (n [%])	
≤2 years	209 (34.4)
>2 years	399 (65.6)
Mean duration of impaired morning function (min [SD])	82.2 (63.0)
Median duration of impaired morning function (min [range])	60 (<10 to 180)
Duration of impaired morning function (n [%])	
≤1 h	355 (58.4%)
>1 h	253 (41.6%)
Mean severity of morning stiffness (score [SD])	6.2 (1.8)
Morning stiffness severity (n [%])	
Mild	45 (7.4)
Moderate	429 (70.6)
Severe	132 (21.7)
RA: Rheumatoid arthritis; SD: Standard deviation.	

Ability to perform morning activities Overall, only around one in three respondents was still able to get ready for the day unimpaired. As severity of morning stiffness increased, there was a significant adverse impact on ability to perform routine activities (p < 0.05 for severe vs moderate and mild morning stiffness; FIGURE 2). Significantly more respondents in paid employment were able to carry out morning activities unimpaired compared with those unable to work due to ill health (p < 0.05; TABLE 2). There were also some significant differences in ability to carry out routine morning activities in subgroups defined according to duration of functional impairment in the morning and age. The duration of disease had little effect on the proportion of patients able to carry out any of the morning activities (data not shown).

Impact of impaired morning function on quality of life

Overall, more than eight out of ten respondents (84%) agreed (somewhat or completely) that impaired morning function had a significant effect on their quality of life; 60% agreed

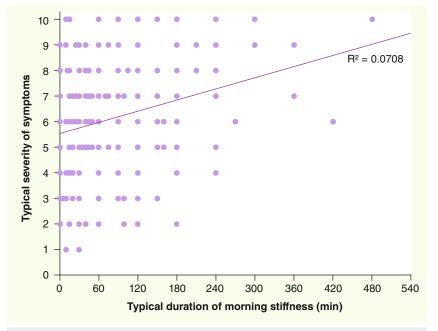


Figure 1. Association between duration of impaired morning function and severity of morning stiffness.

that it controlled their life, 48% that it affects their relationships, 43% that it is difficult to manage and 40% that they feel like a burden due to impaired morning function. The impact of impaired morning function on all aspects of quality of life assessed showed significant (p < 0.05) variation according to severity of morning stiffness (FIGURE 3). The duration of functional impairment in the morning and nonworking status due to ill health both showed a marked impact on aspects of quality of life (TABLE 3). There were no significant differences in responses from subgroups defined by duration of RA (data not shown). Subgroups defined by age range showed no significant differences in response, with the exception of greater impact of morning functional impairment on quality of life in those aged 56–65 years, and it controls life more in those aged 46-65 years, compared with respondents aged 18-45 years (data not shown).

Employment status

Both severity of morning stiffness and duration of impaired function in the morning showed a significant association with work status, although it should be noted that these data are cross-sectional and it is not possible to identify any causal associations. Mean (SD) severity of morning stiffness was significantly (p < 0.05) lower among working respondents (5.8 [1.7]) than those not working due to ill health, retirement or other reasons (6.5 [1.8], 6.7 [1.9] and 6.4 [1.6], respectively). Mean [SD] duration of impaired morning function was significantly (p < 0.05) longer among respondents not working due to ill health (106.8 [78.5] min) than in workers, retired people and those not working for other reasons (73.4 [53.5], 74.2 [54.3] and 79.2 [60.8] min, respectively).

There was a marked impact of morning stiffness on employment status. Fewer than a third of those with severe morning stiffness were in paid work (30%), significantly less than the 48% with moderate morning stiffness and 58% with mild morning stiffness (p < 0.05). Employment fell from 50% of those with impairment of morning function lasting for up to 1 h to 38% of those with prolonged functional impairment (p < 0.05). Conversely, significantly (p < 0.05) more patients with severe morning stiffness (26%) were retired due to ill health than with moderate or mild morning stiffness (both 11%). Retirement due to ill health increased from 11% of those with impaired morning function lasting for up to an hour to 20% of those with prolonged impairment (p < 0.05). Although there were no significant differences in the proportion of patients on sick leave in other subgroups, significantly (p < 0.05) more patients with prolonged functional impairment in the morning (11%) were on sick leave compared to those with impairment lasting up to an hour (6%).

Among the 138 respondents not working due to ill health (i.e., retired early on health grounds and on sick leave), 80% reported that this was because of RA, while nearly half (48%) of the homemakers, students or unemployed reported that they were not working because of RA.

Impact of impaired morning function on work

Among the 271 respondents in paid employment, three-quarters (74%) reported that impaired morning function had a significant impact on their job. Although there were no significant differences across other subgroups, this proportion was significantly (p < 0.05) higher in those with moderate or severe morning stiffness than among those with mild morning stiffness (FIGURE 4). Likewise, significantly (p < 0.05) more patients with moderate or severe morning stiffness reported being unable to work due to morning disability than those with mild morning stiffness, although there were no differences related to duration of functional impairment in the morning or age. However, 52% of the 163 patients with RA for more than 2 years reported being unable to work due to impaired morning function compared with 38% of the 108 working

patients with recent onset disease (p < 0.05). As severity of morning stiffness increased, there were trends towards an increasing proportion of patients reporting slowing of career, need to change job and being made redundant because of impaired morning function, but differences did not reach statistical significance, possibly because of the small numbers of patients affected.

Among working respondents, 41% reported losing one or more days from work during the last 6 months owing to impairment of function in the morning. There were no differences in this proportion across subgroups defined by age, duration of RA or duration of functional impairment in the morning. However, significantly (p < 0.05) fewer patients with mild morning stiffness (12%) lost time off work because of impaired morning function, compared with those with moderate or severe morning stiffness (both 44%). Likewise, the mean (SD) days lost from work among all working respondents with mild morning stiffness (0.5 [2.0] days) was significantly (p < 0.05) lower than for those with moderate (5.1 [13.0] days) or severe (4.5 [7.5] days) morning stiffness.

Discussion

This pan-European survey suggests that patients with RA and impaired morning function experience marked adverse impact on their ability to carry out normal morning activities, quality of life and working life. Subgroup analysis suggests that the impact is more closely associated with the severity of morning stiffness than with age or disease duration.

Although it provides a useful insight, the study has a number of limitations. Causal relationships between morning stiffness and impaired morning function cannot be assumed, as patients with active disease may have both severe morning stiffness and functional impairment in the morning, with disease severity the dominant causal factor. The patients surveyed all experienced impaired morning function (defined as arising from stiffness and pain in the joints, particularly the hands) at least three times a week, so the findings cannot be extrapolated to an unselected population of patients with RA. However, many patient characteristics in this survey appear comparable to those of patients in unselected RA patient populations, possibly reflecting the widespread occurrence of morning symptoms. There were similarities in the proportion of females included (75 vs 79%), mean disease duration (8.1 vs 11.2 years) and mean age of respondents (48.9 vs 56.1 years) in this survey compared with the QUEST-RA database [2]. Interestingly, the mean duration of impaired morning function was approximately half an hour longer in the respondents to this survey than the duration of morning stiffness reported by patients in the QUEST-RA database (82 vs 55 min), possibly reflecting the difference between assessment of outcome and symptom.

An important limitation of any observational study, such as this survey, is the effect of

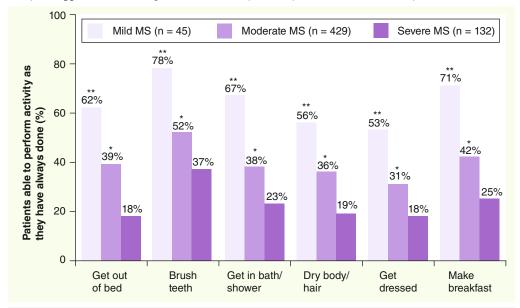


Figure 2. Ability to perform morning activities unimpaired according to severity of morning stiffness.

p < 0.05 vs severe MS; p < 0.05 vs moderate and severe MS. MS: Morning stiffness.

Table 2. Ability to perform morning activities unimpaired according to age range, rheumatoid arthritis duration and work status.

Characteristic n Ge	et out of bed	Brush teeth	able to perform Get in bath/	activities as they	-	ne (%)			
Ge			Get in bath/	Durich a du cha tu					
			shower	Dry body/hair	Get dressed	Make breakfast			
Total 608 36	5	51	37	34	30	40			
Age range (years) *p < 0.05 vs 18–45 years; **p < 0.05 vs 18–45 & 46–55 years									
18–45 197 44	4	57	45	41	38	43			
46–55 193 36	5 .	49	37	36	29	41			
56-65 218 30)*	46*	30*	25**	23*	38*			
Duration of impaired morning function *p < 0.05 vs ≤1 h									
≤1 h 355 38	3	51	41	37	33	44			
>1 h 253 34	1	50	31*	28*	26	36			
Work status *p < 0.05 vs paid work; **p < 0.05 vs not working due to ill health									
Paid work 271 45	ō	60	48	44	39	50			
Not working 138 23 due to ill health	3* .	43*	23*	24*	17*	33*			
Retired 66 32	2	44*	36**	23*	24*	39			
Other 133 35 ³	5*,**	42*	31*	29*	26*	29*			

confounding factors. Stratification of the population by the presence of potential confounding factors is one method of addressing this issue [15]. A similar pattern of responses across strata would indicate confounding, whereas distinct patterns would suggest the factors studied have independent effects (although there may be other confounding factors not assessed in the stratification). A stratification approach was taken in the current survey by assessing the responses in subgroups of the population, defined according to age range, disease duration, severity of morning stiffness and duration of morning functional impairment. Although respondents with recently diagnosed RA or with mild morning stiffness were younger than those with RA for more than 2 years or with severe morning stiffness, different patterns of response were observed. This suggests limited confounding from the factors considered. As an exploratory descriptive study, multivariate analysis was not carried out to assess correlations between factors, though this would be required for any follow-up study.

The survey was conducted by telephone, as a cost-effective method to assess the experience of a large cohort of 750 patients (with this analysis focusing on findings from the 608 patients of working age). The nature of telephone interviews imposes a time constraint on the number and type of question that can be asked. Consequently, the survey was limited in scope, with a focus on the impact of morning symptoms, without a

detailed examination of the relative contribution made from symptoms traditionally considered as distinct (e.g., pain, stiffness, swelling). This prevents a full understanding of the characteristics of this cohort, and means that the findings cannot be placed in the context of other symptoms. The experience of patients reflects the summation of all symptoms. To go some way to address this issue within the practical constraints of the method, the survey focused on the impairment of morning function, considered to be the sum of all symptoms that occur in the morning. However, as an exploratory study, there was no attempt to validate the approach. It should be noted that a rigorous and validated composite measure under development to assess the impact of RA from the patient's perspective (Rheumatoid Arthritis Impact of Disease) does not include morning stiffness or other temporal characteristics of the disease [16,17].

Despite the limitations in the study identified and discussed above, the results suggest that functional impairment in the morning, arising from joint stiffness and pain, has an important impact on the lives and wellbeing of patients. Only around a third of patients included in the survey were able to carry out unimpeded activities that are associated with starting the day, with a marked decline as severity of morning stiffness increased. The survey appears to distinguish between activities involving mobility (e.g., getting out of bed, into the shower/bath, dried and dressed) and those involving dexterity (e.g., brushing teeth and making breakfast). Although there was a significant impact of severity of morning stiffness on both types of activities, the absolute level of impairment was considerably less for activities primarily involving the hands compared with activities involving mobility. This finding is somewhat surprising, given the high level of hand and wrist involvement in RA [18,19]. Impaired hand function has also been cited as the main reason that institutional care is required for people with RA [20]. The findings from this survey highlight the importance of assessing the patient perspective and not deriving assumptions from the main sites of joint damage apparent from imaging.

If key activities such as getting bathed/ showered, dried and dressed present a problem to people with severe morning stiffness, it would not be surprising if they had difficulty being able to get to work. This may be a reason for the association between severe morning stiffness and early retirement from work seen among patients with RA [12]. The findings from this survey are consistent with the view that morning stiffness contributes to loss of employment. The survey also found a marked impact of impaired morning function on patient quality of life, which increased with increasing severity of morning stiffness.

A relationship between severity and duration of morning stiffness has been noted previously [12]. In this survey, the duration of morning stiffness per se was not assessed, although respondents were asked about how long impairment of function lasted in the morning, with limited association observed with severity of morning stiffness. Nevertheless, this survey suggested that severe morning stiffness and prolonged impairment of morning function have subtly different impacts on patients. While it is possible that the dichotomous categories chosen for subgroup analysis of duration of functional impairment (≤ 1 or >1 h) did not adequately reflect the differential impact on patients, there appeared to be more effect of severe morning stiffness on patients than prolonged functional impairment (>1 h). Interestingly, patients are willing to pay more for a reduction in severity of morning stiffness than a reduction in duration of morning stiffness [21]. Despite the predominance of duration of morning stiffness as a measure of the symptom [22], severity has been shown to be a more useful measure [23] that is more closely associated with important outcomes, such as early retirement from work [12].

The findings from the current study suggest that morning stiffness should remain an important consideration when treating patients with RA,

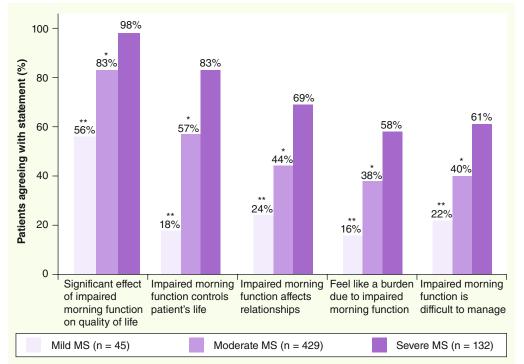


Figure 3. Impact of impaired morning function on aspects of quality of life according to severity of morning stiffness.

p < 0.05 vs severe MS; p < 0.05 vs moderate and severe MS. MS: Morning stiffness.

Table 3. Impact of impaired morning function on aspects of quality of life according to age range, duration of rheumatoid arthritis and work status.

	n	Mean score (standard deviation)								
		Significant effect of impaired morning function on quality of life	Impaired morning function controls patient's life	Impaired morning function affects relationships	Feel like a burden due to impaired morning function	Impaired morning function is difficult to manage				
Total	608	3.21 (0.85)	2.66 (1.02)	2.41 (1.10)	2.23 (1.10)	2.48 (1.01)				
Severity of morning stiffness *p < 0.05 vs mild; **p < 0.05 vs mild & moderate										
Mild	45	2.44 (1.01)	1.73 (0.97)	1.77 (1.00)	1.62 (0.91)	1.84 (1.01)				
Moderate	429	3.14 (0.82)*	2.60 (1.00)*	2.34 (1.07)*	2.17 (1.07)*	2.39 (0.98)*				
Severe	132	3.70 (0.54)**	3.19 (0.84)**	2.87 (1.05)**	2.65 (1.11)**	2.99 (0.87)**				
Duration of	impaired	I morning function *	o < 0.05 vs ≤1 h							
≤1 h	355	3.10 (0.84)	2.56 (1.00)	2.33 (1.06)	2.12 (1.07)	2.39 (0.97)				
>1 h	253	3.36 (0.84)*	2.80 (1.04)*	2.53 (1.14)*	2.39 (1.13)*	2.60 (1.05)*				
Work status	*p < 0.0	5 vs paid work								
Paid work	271	3.11 (0.80)	2.51 (0.97)	2.34 (1.04)	2.08 (1.00)	2.38 (0.92)				
Not working due to ill health	138	3.41 (0.89)*	2.86 (1.08)*	2.52 (1.20)	2.53 (1.20)*	2.61 (1.10)*				

Agreement with statements (score) was rated on a four-point scale (ranging from 1: completely disagree, to 4: completely agree).

despite the exclusion of this common symptom as a criterion in the recent classification criteria for the disease [24] and its lack of assessment in the majority of recent therapeutic trials for RA [5,6]. But current treatment options for morning stiffness are limited [25]. Information about treatment for RA was not collected in this survey, so any impact on functional ability could not be assessed. As noted above, morning stiffness is a key factor in early retirement [12], yet work disability has not been reduced since the introduction of the biological therapies for RA [26]. Biological treatments are also rarely used specifically to treat impaired morning function [25]. Nonpharmacological approaches, including having a warm bath or shower, are the most common management strategies for morning stiffness recommended by rheumatologists [25]. Yet as shown in this survey, getting into a bath or shower presents a considerable problem to patients with impaired morning function. Recent progress in understanding the circadian changes that cause morning symptoms has suggested a new approach that takes into account the timing of treatment [27]. Administration of low-dose glucocorticoid during the night reduces the duration of morning stiffness in comparison to the same dose of glucocorticoid

administered in the morning at the conventional time [28], as does a modified-release preparation of prednisone that is taken at bedtime and gives programmed delivery of active drug approximately 4 h after ingestion [29–31].

Conclusion

In conclusion, this survey has shown that functional disability arising from morning stiffness and pain has a significant impact on tasks associated with starting the day. The impact increases with the severity of morning stiffness. Impaired morning function also has a profound effect on patient quality of life and working life, particularly among those experiencing severe morning stiffness.

Future perspective

We anticipate increasing acceptance of the importance of the patient perspective when physicians consider therapy for RA. In the next 5–10 years, ensuring adequate treatment for disease manifestations that limit patients' lives should improve outcomes for patients. In addition to the moral imperative, such an approach is likely to bring economic benefits by enabling patients to continue as active members of the workforce.

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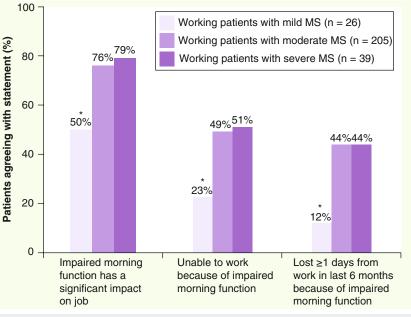


Figure 4. Impact of impaired morning function on work according to severity of morning stiffness.

*p < 0.05 versus moderate and severe MS. MS: Morning stiffness.

Executive summary

Background

• Morning stiffness is a common feature of rheumatoid arthritis (RA), but it is not included in recent RA classification criteria and is now infrequently assessed in clinical trials, although it may impair morning function.

Materials & methods

Patients aged 18–65 years with RA for ≥6 months and impaired morning function arising from joint stiffness and pain more than or equal to three-times a week were interviewed using a structured questionnaire.

Responses were assessed in the total sample and in subgroups defined by severity of morning stiffness.

Results

- A total of 608 respondents completed the questionnaire.
- Only approximately one-third of respondents could perform, unimpaired, morning tasks requiring mobility, with impairment increasing with severity of morning stiffness (p < 0.05).
- Impaired morning function affected quality of life in 84% of respondents, with a significantly greater impact among those with severe compared with mild morning stiffness (98 vs 56%; p < 0.05).</p>
- Only 30% of those with severe morning stiffness were in paid employment versus 48% of those with moderate and 58% of those with mild morning stiffness (p < 0.05).
- Impaired morning function affected the jobs of 74% of the 271 employed respondents (severe morning stiffness: 79 vs mild: 50%; p < 0.05).</p>

Discussion

- As the population studied included only those with impaired morning function, the findings cannot be extrapolated to an unselected patient population, although overall characteristics of the sample were similar to other large surveys of patients.
- There is limited correlation between severity and duration of morning stiffness, and patients are affected differently by prolonged and severe morning stiffness.

Conclusion

- Functional disability arising from morning stiffness and pain has a significant impact on tasks associated with starting the day, which increases with the severity of morning stiffness.
- Impaired morning function has a profound effect on patient quality of life and working life, particularly among those experiencing severe morning stiffness.

Future perspective

Adequate treatment of RA manifestations that affect patients' lives should improve outcomes for patients and allow continued involvement in the active workforce, with the potential for humanistic and economic benefits.

References

Papers of special note have been highlighted as: • of interest

- --- of considerable interest
- Cutolo M, Seriolo B, Craviotto C, Pizzorni C, Sulli A. Circadian rhythms in RA. Ann. Rheum. Dis. 62, 593–596 (2003).
- 2 Khan NA, Yazici Y, Calvo–Alen J *et al.* Reevaluation of the role of duration of morning stiffness in the association of rheumatoid arthritis activity. *J. Rheumatol.* 36, 2435–2442 (2009).
- 3 Yazici Y, Pincus T, Kautiainen H, Sokka T. Morning stiffness in patients with early rheumatoid arthritis is associated more strongly with functional disability than with joint swelling and erythrocyte sedimentation rate. J. Rheumatol. 31, 1723–1726 (2004).
- 4 Felson DT, Anderson J, Boers M et al. The American College of Rheumatology preliminary core set of disease activity measures for rheumatoid arthritis clinical trials. The Committee on Outcome Measures in Rheumatoid Arthritis Clinical Trials. Arthritis Rheum. 36, 729–740 (1993).
- 5 Labitigan M, Sharaf PH, Swearingen C, Yazici Y. Rheumatoid arthritis patients who participated in randomized clinical trials in 1980s versus 2000s: clinical implications of similarities and differences. *Ann. Rheum. Dis.* 69(Suppl. 3), 508 (2010).
- 6 Kalyoncu U, Dougados M, Daures JP, Gossec L. Reporting of patient-reported outcomes in recent trials in rheumatoid arthritis: a systematic literature review. *Ann. Rheum. Dis.* 68, 183–190 (2009).
- 7 Kitamura CR, Rohekar G, Bykerk VP, Carette S. Are the 2002 American College of Rheumatology guidelines for the management of rheumatoid arthritis being followed in Canada's largest academic rheumatology center? J. Rheumatol. 34, 2183–2192 (2010).
- 8 Conway R, Browne P, Low C, Abdul Azeez M, Kearns G, O'Connell P. An audit of documentation in rheumatoid arthritis patients. *Ann. Rheum. Dis.* 69(Suppl. 3), 473 (2010).
- 9 Plant MJ, O'Sullivan MM, Lewis PA, Camilleri JP, Coles EC, Jessop JD. What factors influence functional ability in patients with rheumatoid arthritis. Do they alter over time? *Rheumatology* 44, 1181–1185 (2005).
- 10 Sokka T. Morning stiffness and other patientreported outcomes in rheumatoid arthritis. *Scand. J. Rheumatol.* 40(Suppl. 125), 23–27 (2011).

- Sokka T, Haugeberg G, Pincus T. Assessment of quality of rheumatoid arthritis care requires joint count and/or patient questionnaire data not found in a usual medical record: examples from studies of premature mortality, changes in clinical status between 1985 and 2000, and a QUEST-RA global perspective. *Clin. Exp. Rheumatol.* 25(6 Suppl. 47), 86–97 (2007).
- 12 Westhoff G, Buttgereit F, Gromnica–Ihle E, Zink A. Morning stiffness and its influence on early retirement in patients with recent onset rheumatoid arthritis. *Rheumatology* 47, 980–984 (2008).
- Database analysis showing correlation between early retirement and severe morning stiffness.
- 13 Grønning K, Rødevand E, Steinsbekk A. Paid work is associated with improved healthrelated quality of life in patients with rheumatoid arthritis. *Clin. Rheumatol.* 29, 1317–1322 (2010).
- 14 da Silva JAP, Phillips S, Buttgereit F. Impact of impaired morning function on the lives and wellbeing of patients with rheumatoid arthritis. *Scand. J. Rheumatol.* 40(Suppl. 125), 6–11 (2011).
- 15 Psaty BM, Koepsell TD, Lin D et al. Assessment and control for confounding by indication in observational studies. J. Am. Geriatr. Soc. 47, 749–754 (1999).
- Gossec L, Dougados M, Rincheval N *et al.* Elaboration of the preliminary Rheumatoid Arthritis Impact of Disease (RAID) score: a EULAR initiative. *Ann. Rheum. Dis.* 68, 1680–1685 (2009).
- 17 Gossec L, Pattemotte S, Aanerud GJ et al. Finalisation and validation of the rheumatoid arthritis impact of disease score, a patientderived composite measure of impact of rheumatoid arthritis: a EULAR initiative. Ann. Rheum. Dis. 70, 935–942 (2011).
- 18 Adams J, Burridge J, Mullee M, Hammond A, Cooper C. The clinical effectiveness of static resting splints in early rheumatoid arthritis: a randomized controlled trial. *Rheumatology* 47, 1548–1553 (2008).
- Kauranen K, Vuotikka P, Hakala M. Motor performance of the hand in patients with rheumatoid arthritis. *Ann. Rheum. Dis.* 59, 812–816 (2000).
- 20 Sollerman C. The hand. In: Rheumatoid Arthritis: New Frontiers in Pathogenesis and Treatment (1st Edition). Firestein GS, Panayi G, Wollheim FE (Eds). Oxford University Press, Oxford, UK, 467–476 (2000).

- 21 Tuominen R, Tuominen S, Timo M. How much is a reduction in morning stiffness in rheumatoid arthritis worth to patients? *Scand. J. Rheumatol.* 40(Suppl. 125), 12–16 (2011).
- Cutolo M. How should morning function be assessed? Bibliographic study of current assessment. *Scand. J. Rheumatol.* 40(Suppl. 125), 17–22 (2011).
- 23 Hazes JMW, Hayton R, Silman AJ. A reevaluation of the symptom of morning stiffness. J. Rheumatol. 20, 1138–1142 (1993).
- 24 Aletaha D, Neogi T, Silman AJ et al. 2010 rheumatoid arthritis classification criteria. Arthritis Rheum. 62, 2569–2581 (2010).
- 25 Buttgereit F. How should impaired morning function in rheumatoid arthritis be treated? *Scand. J. Rheumatol.* 40(Suppl. 125), 28–39 (2011).
- 26 Sokka T, Kautiainen H, Pincus T *et al.* Work disability remains a major problem in rheumatoid arthritis in the 2000s: data from 32 countries in the QUEST-RA study. *Arthritis Res. Ther.* 12, R42 (2010).
- 27 Straub RH, Cutolo M. Circadian rhythms in rheumatoid arthritis: implications for pathophysiology and therapeutic management. *Arthritis Rheum.* 56, 399–408 (2007).
- Useful review providing an introduction to circadian features of rheumatoid arthritis.
- 28 Arvidson NG, Gudbjörnsson B, Larsson A, Hällgren R. The timing of glucocorticoid administration in rheumatoid arthritis. *Ann. Rheum. Dis.* 56, 27–31 (1997).
- First report of improved outcomes when therapy for rheumatoid arthritis is appropriately timed.
- 29 Buttgereit F, Doering G, Schaeffler A et al. Efficacy of modified-release versus standard prednisone to reduce duration of morning stiffness of the joints in rheumatoid arthritis (CAPRA-1): a double-blind, randomised controlled trial. *Lancet* 371, 205–214 (2008).
- 30 Buttgereit F, Doering G, Schaeffler A et al. Targeting pathophysiological rhythms: prednisone chronotherapy shows sustained efficacy in rheumatoid arthritis. Ann. Rheum. Dis. 69, 1275–1280 (2010).
- 31 Kirwan JR, Clarke L, Hunt LP, Perry MG, Straub RH, Jessop DS. Effect of novel therapeutic glucocorticoids on circadian rhythms of hormones and cytokines in rheumatoid arthritis. *Ann. NY Acad. Sci.* 1193, 127–133 (2010).