Original Article

Chi Chiu Mok*, Hoon-Suk Cha, Emmanuel C Perez, Gregory J Tsay, Kam Hon Yoon

Dissonance between physicians’ and patients’ perspectives on managing impaired morning function in Asian patients with rheumatoid arthritis

https://doi.org/10.1515/hkbrd-2017-0002
Received April 5, 2017; accepted May 4, 2017

Abstract: Objectives: To estimate the prevalence of impaired morning function (IMF) in rheumatoid arthritis (RA), and to understand physicians’ and patients’ perceptions on the impact of IMF and treatment in selected Asian countries. Methods: A survey on the impact of IMF was conducted in Asia on rheumatologists and patients with moderate-to-severe RA who experienced IMF for ≥3 mornings a week. Participants underwent comprehensive face-to-face interviews using structured questionnaires. Results: Sixty physicians and 300 patients from Hong Kong, Philippines, Singapore, South Korea, and Taiwan were surveyed. Rheumatologists estimated that two-thirds of patients with RA experienced IMF and believed that the prevalence of IMF increased with RA severity (present in 42%, 73%, and 87% of patients with mild, moderate, and severe disease, respectively). Patients’ survey revealed that, on average, patients with RA experienced IMF 5 days a week for 2 h each day. Thirty-eight percent of patients with RA considered a reduction in morning stiffness as an important treatment goal, but this was agreed by only 3% of rheumatologists. Only 22% of rheumatologists modified the treatment regimen specifically for IMF. Physicians considered prednisolone and other glucocorticoids (GCs) to be the most effective medication for the treatment of IMF. Fifty-one percent of patients with RA did not find their current medication effective in relieving IMF, and as a result, they reported negative emotions such as frustration, defeat, and anger, and 56% had missed work because of this symptom. Conclusions: IMF is prevalent in RA and significantly affects patients’ quality of life (QoL). A higher proportion of patients compared to physicians view the reduction of morning stiffness as an important goal. More should be done to address the dissonance between physicians’ and patients’ views on IMF.

Keywords: Asian, impaired morning function, rheumatoid arthritis, morning stiffness

1 Introduction

Impaired morning function (IMF) due to joint pain and stiffness is a commonly reported feature of rheumatoid arthritis (RA) [1–3]. Up to 69% of patients in the large QUEST-RA database of more than 5,000 patients experienced IMF [4]. IMF occurs irrespective of disease activity and is not restricted to patients with poorly controlled RA. According to the QUEST-RA data, IMF was reported in 44% of patients considered to have low disease activity or in remission [4].

Evidence suggests that IMF has a significant impact on patient’s lives resulting in limited function during the early morning hours. In a pan-European survey, in patients aged 18–75 years with RA of ≥6 months’ duration, the majority of patients (82%) with morning stiffness felt that IMF adversely affected their quality of life (QoL) [5]. Approximately two-thirds of patients reported a need to change with regard to how they performed their usual morning activities. Consequently, patients who were unable to function normally in the morning reported feeling frustrated (58%) and angry (32%). Nearly one in five patients in this survey was unable to work because of IMF [5].
Glucocorticoids (GCs) remain one of the most widely used agents in patients with RA. Low-dose GCs in combination with synthetic disease-modifying antirheumatic drugs (DMARDs), most often methotrexate, significantly improve structural outcomes and decrease symptom severity in patients with RA [6]. Low-dose GCs are recommended by the recent European League Against Rheumatism (EULAR) guidelines as part of the initial treatment strategy in RA (in combination with ≥1 DMARD) for a period of up to 6 months [7]. GCs, including modified-release prednisolone, have been shown to reduce pain and early IMF in patients with RA [8]. However, composite measures to determine treatment efficacy, such as the Disease Activity Score 28 (DAS28), do not include IMF as a domain [9]. Furthermore, IMF is not included in American College of Rheumatology (ACR) classification criteria for RA [10], possibly because of the non-specific nature of this symptom. As IMF is included in neither the assessment tools nor the classification criteria for RA, physicians may overlook IMF symptoms in patients and underestimate the significance of IMF.

It is well established that disease-related symptoms in patients with chronic inflammatory diseases exhibit circadian rhythms. In particular, patients with RA experience joint pain, morning stiffness, and functional disability in the early morning hours [11]. Approximately 50% of patients experience IMF for at least 1 h/day [2, 3]. This circadian pattern correlates with an early morning rise in circulating levels of pro-inflammatory cytokines, such as interleukin (IL)-6, and in the decreased secretion of cortisol, suggesting that clinical symptoms may be related to hormonal and immune circadian variations [12, 13].

At present, there is a lack of information on IMF in Asian patients with RA, particularly with regard to the impact of IMF from the perspectives of both the patient and the physician. Therefore, a multinational survey was conducted to determine the views of Asian rheumatologists and Asian patients with RA on IMF as well as to understand its impact and importance. The survey results collected from patients and physicians were further examined to understand the agreement or dissonance between the two parties.

## 2 Patients and methods

### 2.1 Participants

A survey on the impact of IMF in RA was conducted on 60 rheumatologists and 300 patients with RA from Hong Kong, the Philippines, Singapore, South Korea, and Taiwan. Moderate and severe RA was defined according to the 1991 ACR criteria for the classification of global functional status in RA [14]. Rheumatologists included in the study had to fulfill the following criteria: (1) in public or private practice for at least 5 years; (2) spend ≥70% of clinical practice time in treating patients with RA; (3) treat ≥40 patients with RA in a typical month; and (4) treat ≥20 patients with moderate-to-severe RA in a typical month, with ≥8 patients who experience IMF and require treatment with DMARDs or biologics.

Patients who participated in this survey were referred by the following sources: (1) referral from rheumatologists who participated or did not participate in this survey, (2) self-help groups or associations of patients with RA in the respective Asian countries and (3) referral from rheumatology nurses and patients with RA. Patients were included if they were diagnosed with moderate-to-severe RA for the last at least 6 months, had IMF ≥3 mornings per week and were receiving medications for RA (i.e., DMARDs and/or biologics). IMF was defined as patients’ self-reported stiffness and joint pain in the morning that lasted for >1 h, which resulted in difficulty in functioning or performance of certain tasks. Profile of the patients surveyed is included in Supplementary Information, Appendix 3.

### 2.2 Surveys

Participants underwent comprehensive face-to-face interviews conducted by Frost & Sullivan using structured questionnaires, which consisted of questions in a variety of formats, including open-ended questions. A number of specific issues were evaluated. For rheumatologists, the 20-min survey consisted of 32 questions on physicians’ perspectives in associating IMF with RA (Supplementary Material, Appendix 1). These questions included whether physicians consider IMF to be a problem that is correlated with RA; what treatments physicians prescribe; how they manage IMF; what the physician’s level of satisfaction with current treatments of IMF; and the current unmet needs are. For patients with RA, the 20-min survey consisted of 33 questions on the impact of IMF on their daily functions, emotions and QoL (Supplementary Material, Appendix 2). These questions included perceived priority for improving the overall QoL in the treatment of RA (e.g., reduction in joint pain or morning stiffness); IMF; emotional disturbances related to IMF (e.g., feeling frustrated, angry, or tired); the impact of IMF on activities of daily living and work; and the efficacy of treatment of IMF given by physicians.
2.3 Statistical analysis

Sample size calculation was based on the incidence rate of the use of DMARDs and biologics in patients with RA. Data presented in this study were expressed as mean (standard deviation) for continuous variables and percentages for discrete values. For the part of survey on rheumatologists, demographic data were categorized according to country and the type of practice. For the part of survey on patients, demographic data were categorized according to country, severity of RA, and the use of medications (DMARDs vs. biologics).

3 Results

A total of 60 physicians and 300 patients were surveyed (Table 1). On an average, each rheumatologist treated 174 patients with RA per month, of whom 44% had moderate RA and 25% had severe RA. Of the 300 patients with RA surveyed, 69% had moderate RA and 95% were receiving DMARD therapy.

3.1 IMF prevalence

Overall, rheumatologists estimated that 67% of their patients with RA experienced morning stiffness, with the prevalence of IMF correlating with RA severity. They believed that IMF was present in 42%, 73%, and 87%, respectively, of patients with mild, moderate, and severe RA. Sixty-seven percent of rheumatologists used the duration of morning stiffness to assess the severity of IMF. There was an agreement between the physician and patient surveys regarding the duration of IMF: around 5 days a week for approximately 2 h, on an average.

3.2 IMF significantly affects patient’s quality of life

IMF has considerable impact on the physical function and emotion of patients with RA. Feeling of being frustrated, defeated, anger, and emotionally drained was reported in 68%, 38%, 35%, and 31% of the patients with RA, respectively. Pain and stiffness were the most common physical symptoms that were experienced by 83% and 82% of patients, respectively. A total of 55% of patients with RA reported that the pain experienced as a result of stiffness was the most distressing component of IMF. More than 60% of patients reported that IMF had a significant impact on their QoL. Approximately half of the patients surveyed (47%) found getting out of bed difficult because of IMF but they did not require assistance to get out of bed. A number of tasks were identified as being more difficult because of IMF. These included getting dressed, making breakfast, and looking after their children’s needs in the morning. As a result of IMF, 15–22% of patients required assistance to get dressed, to make breakfast, and to look after their children’s needs in the morning (Figure 1); 63% of patients needed help to complete household chores; and 40% were unable to work (Figure 2). The majority of patients (56%) had missed work because of IMF (Figure 2), for a mean of 6.9 days in the past 6 months because of IMF.

3.3 Patients were more likely to view morning stiffness as an important treatment goal

The majority of physicians (90%) did not consider the duration of morning stiffness as a criterion for categorizing the severity of RA, though 78% of them asked specifically

| Table 1: Demographic data of the survey respondents |
|---------------------------------|---------|--------|---------|---------|---------|
| **Country** | **Physicians** | **Patients** | **Severity of RA** | **Treatment (n)** |
|       | **N (%)** | **N (%)** | **Moderate** | **Severe** | **DMARDs** | **Biologics** |
| Hong Kong | 9 (15) | 35 (12) | 29 | 6 | 34 | 6 |
| Philippines | 12 (20) | 80 (26) | 55 | 25 | 80 | 3 |
| Singapore | 9 (15) | 40 (13) | 27 | 13 | 35 | 6 |
| South Korea | 16 (27) | 70 (23) | 55 | 15 | 67 | 13 |
| Taiwan | 14 (23) | 75 (25) | 41 | 34 | 70 | 44 |
| Total | 60 (100) | 300 (100) | 207 | 93 | 286 | 72 |
Impaired Morning Function in Asian Patients with RA

Table 1: Demographic data of the survey respondents

<table>
<thead>
<tr>
<th>Country</th>
<th>Physicians N (%)</th>
<th>Patients N (%)</th>
<th>Severity</th>
<th>Treatment (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Moderate</td>
<td>Severe</td>
<td>DMARDs</td>
<td>Biologics</td>
</tr>
<tr>
<td>Hong Kong</td>
<td>9 (15)</td>
<td>35 (12)</td>
<td>29</td>
<td>6</td>
</tr>
<tr>
<td>Philippines</td>
<td>12 (20)</td>
<td>80 (26)</td>
<td>55</td>
<td>25</td>
</tr>
<tr>
<td>Singapore</td>
<td>9 (15)</td>
<td>40 (13)</td>
<td>27</td>
<td>13</td>
</tr>
<tr>
<td>South Korea</td>
<td>16 (27)</td>
<td>70 (23)</td>
<td>55</td>
<td>15</td>
</tr>
<tr>
<td>Taiwan</td>
<td>14 (23)</td>
<td>75 (25)</td>
<td>41</td>
<td>34</td>
</tr>
<tr>
<td>Total</td>
<td>60 (100)</td>
<td>300 (100)</td>
<td>207</td>
<td>93</td>
</tr>
</tbody>
</table>

For the duration of morning stiffness when assessing disease severity during consultations (Figure 3). Only 3% of physicians ranked reducing morning stiffness as an important treatment goal, while the proportion of patients who ranked a reduction in morning stiffness as an important treatment target was 10 times higher (38% vs. 3%; Figure 4).

While 90% of rheumatologists felt the current treatment options available for IMF were already effective, 75% of patients were eagerly looking for a solution for...
Chi Chiu Mok, et al.

However, 78% of rheumatologists believed that no specific treatment for IMF is required and that treating RA-related pain is more important than morning stiffness. Most physicians (73%) believed that the treatments they are currently prescribing for RA should also be able to manage IMF. More than one-third (38%) of physicians also believed that IMF should be accepted as part of the patient’s condition. In contrast, 91% of patients with IMF expected reduction in joint pain as the main treatment goal, while 86% of patients expected a reduction in morning stiffness after treatment.

### 3.4 Few physicians prescribe treatment specifically for IMF

The application of heat, taking a hot bath and practicing short, simple exercises were the two main strategies for alleviating IMF according to both the rheumatologists and the patients (Figure 5). However, there appears to be some dissonance between patients and physicians with regard to their views on medical treatment. Only 22% of physicians prescribed medications specifically for IMF. However, 40% of patients interviewed reported that they received medication specifically for IMF. A minority of physicians (15%) recommended alternative treatment options (e.g., switch in current medication, addition of other drugs to existing medication, or dose adjustments of current medication), while 31% of patients reported that they were offered an alternative treatment option (Figure 5).

A total of 85% of patients took prescribed medications to relieve IMF, but 51% of patients did not find their current medications effective for relieving IMF. Only 14% of patients were satisfied with the efficacy of medications for IMF. Of the patients who did not take any medications...
for IMF, 68% were not aware of the availability of such medications. The majority of patients (81%) were willing to pay (up to US$1 per day) for medications to relieve IMF, if any.

More than 70% of physicians would prescribe a marketed product for the treatment of IMF. Of the seven physicians who would not prescribe medications for IMF, 71% of them mentioned that IMF can be easily managed if RA-related inflammation can be controlled.

### 3.5 Attitudes toward glucocorticoids

In total, 58% of physicians considered prednisolone and other GCs to be the most effective medication for the treatment of IMF. Key barriers to the prescription of GCs included weight gain, hyperglycemia and osteoporosis. However, there were no recommendations on the optimal dose, duration, and tapering of GCs for IMF.

Rheumatologists prescribed GCs to 64% of their patients for disease control. The usual starting dose was 10 mg/day and the maintenance dose was 5 mg/day. Overall, 58% of rheumatologists split the dose of GCs for RA, with 57% prescribing half of the dosage in the morning and half in the evening. The most common reason for splitting the dose of GCs was to help reduce stiffness in the morning (32%).

### 4 Discussion

Despite evidence from a large database of more than 5,000 patients demonstrating that IMF is a significant issue for patients with RA [4], there is limited information on IMF in Asian patients with RA, particularly with regard to physician’s and patient’s perceptions. The current survey was designed to assess the prevalence of IMF in patients with RA in Asia and to evaluate sources of dissonance between patients and physicians. This study has a number of inherent strengths. It is a large multinational survey that incorporated the perceptions of rheumatologists from both the private and public sectors. It is also one of the first such studies examining attitudes towards IMF in RA in Asia. However, this study is limited by a potential source of selection bias because patient recruitment largely relied on referrals by rheumatologists. The study also has inherent indication bias, as it surveyed only patients with moderate-to-severe RA who experienced IMF for at least three mornings per week. Therefore, the findings only apply to patients with RA who experience IMF.

![Figure 5. Rheumatologists’ Advice to RA patients to deal with morning symptoms and subsequent action taken by patients](image-url)
In the current study, the perceived prevalence of IMF was 67%, with patients experiencing IMF for an average of 5 days per week. IMF lasts for an average of 2 h each morning and exhibits significant negative impact on the daily activities of patients. This is similar to the finding by the OMERACT group that stiffness has an independent effect on multiple dimensions of health, including physical, emotional, and social health [15]. The group also stated that more research on stiffness measurement is needed, as duration and intensity may not be sufficient to reflect the complexity of the experience [15].

In addition, there appears a significant degree of discordance between patients and physicians’ perception of IMF, specifically morning stiffness. Discrepancies between the perception of disease activity between patients and physicians have been reported in an earlier study [16]. Studenic et al. found that the duration of morning stiffness is one of the variables highly associated with the degree of discrepancy between the patient global assessment and evaluator’s global assessment [16].

A reduction in morning stiffness was a more important treatment consideration according to the patients with RA as compared to the physicians. While rheumatologists acknowledged that a large proportion of their patients with moderate-to-severe RA experience IMF and that IMF has a significant impact on patients’ QoL, they do not appear to view it as a treatment priority. Most rheumatologists believe that morning stiffness or IMF are normal components of RA; hence, treating RA-related pain is more important. On the contrary, patients reported significant emotional impact owing to IMF, which caused anger and frustration.

Although IMF is not considered to be a serious concern by the rheumatologists, the impact of IMF on patients is high. As a result of IMF, up to 60% of patients cannot get out of bed easily and almost two-thirds of them require assistance to complete daily household chores. Furthermore, more than half of the patients surveyed suffered from work disability attributed by IMF. As this survey mainly focused on self-reported symptom of IMF from the patients, we did not have information on their disease activity status. It remains possible that concomitant arthritis may have contributed to the missed work, among other psychosocial factors.

From the patients’ perspective, there is a need for effective treatment for IMF. However, 38% of rheumatologists stated that patients should accept that IMF is part of their RA condition so that IMF is not treated specifically. Furthermore, 33% of rheumatologists commented that current treatment options do not specifically address IMF. For the treatment of IMF, physicians generally tend to increase the dosage of current treatment or add on another DMARD for general RA activity. Most of the physicians add GCs to the existing RA treatment regime to address IMF.

The 2014 EULAR guidelines state that low-dose GCs should be considered as part of the initial treatment strategy for RA [7]. The efficacy and tolerability of low-dose modified-release prednisolone in the treatment of IMF has been demonstrated in two clinical studies involving more than 600 patients with RA [17, 18]. Modified-release prednisone is more efficacious than the immediate release form in reducing the duration of morning stiffness [17]. Addition of modified-release prednisolone to DMARDs was shown to produce higher response rates for ACR20, ACR50 and reduction in morning stiffness, compared with DMARDs and placebo [18]. With the available evidence, physicians may consider treating patients with IMF, as most patients regard IMF a significant concern of their illness and they are ready to shoulder the cost of the medications. Our survey identified that the key barriers to the prescription of GCs were weight gain, hyperglycemia, and osteoporosis. In fact, low-dose and short-term GCs are not often associated with these side effects.

In conclusion, IMF has significant impact on QoL and patients with RA perceive a strong need for an effective treatment. However, only 22% of rheumatologists prescribe medications specifically for IMF. Physicians should consider prescribing evidence-based treatment for IMF.

Funding Source and Declaration of Financial Interests: Mundipharma Pte Ltd provided a grant for the survey and for medical writing support of this manuscript. All authors do not have any conflict of interests to be declared.

References


