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ORIGINAL RESEARCH

Demographic, Physical, and Psychological Determinants of Patient Experience with Subcutaneous Self-Injection in Patients with Rheumatoid Arthritis: Structural Equation Modeling Approach

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Purpose: To achieve a better patient experience with self-injection, an assessment of potential demographic, physical, and psychological barriers is necessary. The aim of this study was to examine the demographic, physical, and psychological characteristics associated with the experiences of self-injection in patients with rheumatoid arthritis (RA).

Patients and Methods: In this study, overall patient experience with subcutaneous self-injection was assessed using the Self-Injection Assessment Questionnaire. Upper limb function was assessed using the three domains of the Health Assessment Questionnaire associated with upper extremity disability (dressing and grooming, eating, and grip). Structural equation modeling was used to estimate the association between the demographic and clinical characteristics of patients with RA and their experiences with self-injection in the theoretical model.

Results: Data from 83 patients with RA were analyzed. Compared with younger patients, elderly patients were more likely to experience lower self-confidence, self-image, and ease of use. Female patients had lower ease of use than male patients. In terms of upper limb function, patients with more difficulty in performing activities of daily living were more likely to have a lower self-image. Self-injection perceptions before learning the method of injection, such as fear of needles and anxiety about self-injection, were associated with post-injection feelings, injection site reactions, self-confidence, and ease of use.

Conclusion: To optimize patients' experiences with self-injection, healthcare workers should assess each patient's age, sex, upper limb function, and pre-self-injection perceptions as demographic, physical, and psychological barriers.

Keywords: rheumatoid arthritis, self-injection, biologics, self-injection assessment questionnaire

Background

Rheumatoid arthritis (RA) is a chronic autoimmune and inflammatory disease that is associated with joint inflammation, pain, structural damage, and impaired physical function. This can lead to increased morbidity and mortality, and long-term treatment is required.[1] Biological disease-modifying anti-rheumatic drugs (bDMARDs) have been demonstrated to improve disease activity, structural damage, physical function, and quality of life[2] and they may be administered by subcutaneous injection or intravenous infusion. The intravenous route requires frequent clinic or hospital visits for regular injections and places a greater economic burden on both the patient and the healthcare system. In contrast,

Received: 12 April 2023
Accepted: 30 May 2023
Published: 3 July 2023

subcutaneous injection allows self-administration and is likely to provide patients with control of the treatment schedule (within the limits allowed by physicians) and setting. Self-injection may also provide psychological benefits and increase self-esteem.[3] There are, however, several physical and psychological barriers to their self-injection.[4] Potential physical barriers include hand dexterity problems due to structural damage in the hand and disability of the upper extremity, while psychological and social barriers may include injection anxiety, lack of confidence in self-injection, and potential embarrassment associated with self-injecting in public.

Better patient experience with self-injection leads to a greater likelihood of adherence to a self-injection regimen.[5] When physicians, nurses, and pharmacists educate and support patients about self-injection techniques, they need to assess potential physical and psychological barriers to achieve better patient experiences with self-injection. However, no studies have evaluated the relationship between the demographic and clinical characteristics of patients with RA and their experiences with self-injection.

Therefore, this study aimed to examine the demographic, physical, and psychological characteristics associated with patients' experiences with self-injection in patients with RA.

Materials and Methods

Participants and Study Design

We used data from an observational study performed at a tertiary center, Kobe University Hospital between October 2019 and March 2022.[6] During this period, 867 patients with RA visited the hospital regularly. Patients with RA were consecutively included if they fulfilled the following pre-specified criteria: aged ≥18 years old, diagnosed with RA according to the 2010 American College of Rheumatology (ACR)/European League Against Rheumatism (EULAR) classification criteria,[7] judged by physicians to need a self-injected bDMARD, had no previous experience of self-injection or no experience for >1 year since the last self-injection, and deemed able to read and interpret the questionnaires applied. In this study, four tumor necrosis factor (TNF) inhibitors (etanercept, adalimumab, certolizumab pegol, and golimumab), two interleukin-6 (IL-6) receptor inhibitors (tocilizumab and sarilumab), and one cytotoxic T-lymphocyte-associated protein 4 immunoglobulin (abatacept) were available for self-injection.

Measures/Instruments

Overall patient experience with subcutaneous self-injection was assessed through the Self-Injection Assessment Questionnaire (SIAQ), which is a valid and reliable tool for patients with RA and includes the PRE and POST modules to evaluate the patients' perceptions before and after learning the self-injection method.[8] The PRE module consisted of feelings about injections, self-confidence, and satisfaction with medication, whereas the POST domains included five causal domains (feelings about injections, self-image, self-confidence, injection-site reactions, and ease of use) and satisfaction with self-injection. Feelings about injection included fear of needles, anxiety, and fear of self-injection. Self-image was determined as an embarrassment associated with self-injection in public. Self-confidence estimated one's ability to self-inject correctly. Injection site reactions included pain, unpleasant sensations, and skin reactions. Ease of use assessed how easily a device was used. Satisfaction with self-injection estimated the convenience of the device, ease of self-injection, ease of administration, and willingness to continue self-injection. In the conceptual model of the SIAQ, causal domains affected satisfaction with self-injection. The SIAQ PRE module was self-completed before the first self-injection, and the POST module was self-assessed after nurses provided instructions, and patients completed self-injection. Patients rated each item on a 5-point semantic Likert-type scale, in which a score of 1 corresponded to the patient's worst experience, and a score of 5 corresponded to the patient's best experience. Item scores were transformed to obtain scores ranging from 0 (worst experience) to 10 (best experience) for each item. The domain score was the mean of the item scores included in the domain.

Demographic data, disease characteristics, and current treatments were collected for patient characterization. Disease activity was measured using the Clinical Disease Activity Index (CDAI).[9] To assess difficulty in performing activities of daily living, a health assessment questionnaire (HAQ) was used.[10] Because upper limb function theoretically influenced self-injection, upper limb function was assessed using the three HAQ domains associated with disability of the upper

extremity (dressing and grooming, eating, and grip). Structural damage in the hands was assessed using radiography with a Steinbrocker radiographic stage.[11]

Statistical Analysis

Pearson correlation analyses were conducted to examine the associations between the SIAQ domains, which were interpreted as small (0.10 to 0.30), moderate (0.30 to 0.50), or large (>0.50). Structural equation modeling was used to estimate the association between the observed variables in the theoretical model using maximum-likelihood estimation and Huber-White robust standard errors. Structural equation modeling is a statistical technique used to examine complex relationships among variables. It combines elements of factor analysis and regression analysis to assess both direct and indirect effects between latent and observed variables and tests theoretical models and analyze complex data. The primary goal of structural equation modeling is to estimate and test a hypothesized theoretical model. The model consists of a set of relationships between variables, which are represented through path diagrams or equations. The path diagrams depict the direction and strength of relationships between the variables, including both direct and indirect effects. By using structural equation modeling, researchers can evaluate the overall fit of the model to the data and assess the significance and magnitude of the relationships between variables.[12]

Prior to the analysis, the assumption of multicollinearity was confirmed. The variance inflation factor values were below 3 for all variables included in the model, excluding multicollinearity as an issue. As recommended, the following goodness-of-fit indices were used to estimate the model fit: (1) the χ^2 value, (2) the comparative fit index (CFI), (3) the Tucker-Lewis Index (TLI), (4) the root mean square error of approximation (RMSEA), and (5) the standardized root mean square residual (SRMR). A good fit of the models was assumed when the ratio of χ^2 to its degree of freedom was less than 2.0, and CFI and TLI were larger than 0.95. RMSEA values <0.06 were considered ideal, and values between 0.08 and 0.10 were considered acceptable; SRMR should be <0.10.[13] The examination of the structural model included a test of the overall model fit as well as individual tests of the relationships among variables. Paths with *P*-values of >0.20 were excluded, and the initially proposed model was readjusted accordingly.

The current analysis included data from patients who answered all required measurements. To address potential bias due to missing data, we tested multiple imputation by chained equations, which did not show significant differences. Finally, we preferred to use only truly obtained data. Statistical significance was set at $P < 0.05$. Statistical analyses were conducted using R version 4.1.2 (R Development Core Team, Vienna, Austria).

Results

Patient Characteristics

The baseline demographic and clinical characteristics of the 83 patients with RA are presented in Table 1. The mean age was 63.0 years old, 65% of the participants were female, and the median disease duration was 4.7 years. The mean disease activity was moderate, and 24.7% of the patients had severe structural damage. Most patients were beginning self-injection of bDMARD for the first time and initiated a TNF inhibitor or an IL-6 receptor inhibitor.

The SIAQ domain scores and Pearson correlation coefficients for the domains are presented in Table 2 and Table 3.

As the conceptual model of the SIAQ suggests, five causal domains in the POST module generally correlated with satisfaction with the self-injection domain.

Feelings regarding injections in the PRE module presented moderate to high correlations with all domains in the POST module. Higher self-confidence in the PRE module was associated with higher self-confidence and ease of use in the POST module.

Structural Equation Modeling

The overall fit of the final measurement model was good, thus permitting the examination of the structural model ($\chi^2_{(32)} = 31.5$; χ^2/degree of freedom = 0.98; $P = 0.49$; CFI = 1.00; TLI = 1.00; RMSEA = 0.00, 90% confidence interval [CI], 0.00 to 0.09; SRMR = 0.06).

Table 1 Patient Characteristics at Baseline

Patients with Rheumatoid Arthritis	N = 83
Age (years, SD)	63.0 ± 13.8
Sex (female, %)	65 (78.3)
Anti-citrullinated peptide antibody (n, %)	66 (82.5)
Rheumatoid factor (n, %)	61 (77.2)
Disease duration (years, IQR)	4.7 (1.5, 11.5)
Clinical disease activity index (IQR)	11.8 (5.3, 19.4)
Health assessment questionnaire (IQR)	0.6 (0.2, 1.1)
Steinbrocker classification (Stage III/IV, %)	20 (24.7)
Type of biological DMARDs (n, %)	
CTLA-4 immunoglobulin	11 (13.3)
IL-6 receptor inhibitor	34 (41.0)
TNF inhibitor	38 (45.8)
Biological DMARD-naive (n, %)	73 (88.0)
Corticosteroid use (n, %)	40 (48.2)
Methotrexate use (n, %)	39 (47.0)
Sulfasalazine use (n, %)	22 (26.5)
Other conventional synthetic DMARD use (n, %)	38 (45.8)

Notes: Continuous variables were expressed as mean ± SD or median (IQR).
Abbreviations: SD, standard deviation; IQR, interquartile range; DMARD, disease-modifying antirheumatic drug; CTLA-4, cytotoxic T-lymphocyte-associated protein 4; IL-6, interleukin-6; TNF, tumor necrosis factor.

Table 2 Self-Injection Assessment Questionnaire (SIAQ) Domain Scores

Patients with Rheumatoid Arthritis		Naïve User	Previous User
	83	73	10
SIAQ PRE module			
Feelings about injections (IQR)	7.5 (5.0, 8.3)	7.5 (5.0, 8.3)	7.5 (6.7, 8.3)
Self-confidence (IQR)	5.0 (3.3, 5.0)	5.0 (3.3, 5.0)	5.0 (3.5, 5.6)
Satisfaction with medication (IQR)	5.0 (5.0, 7.5)	5.0 (5.0, 7.5)	5.0 (5.0, 5.0)
SIAQ POST module			
Feelings about injections (IQR)	7.5 (6.7, 8.3)	7.5 (5.8, 8.3)	7.9 (7.5, 8.3)
Self-image (IQR)	10.0 (7.5, 10.0)	10.0 (7.5, 10.0)	7.5 (7.5, 10.0)
Self-confidence (IQR)	5.0 (4.6, 6.7)	5.0 (4.2, 6.7)	5.0 (5.0, 7.5)
Injection site reactions (IQR)	9.6 (9.2, 10.0)	9.6 (9.2, 10.0)	9.6 (9.3, 9.6)
Ease of use (IQR)	7.2 (5.2, 8.8)	7.2 (4.8, 8.8)	6.4 (5.6, 7.6)
Satisfaction with self-injection (IQR)	6.1 (5.4, 7.3)	6.1 (5.4, 7.5)	5.9 (5.7, 6.8)

Notes: Continuous variables were expressed as median (IQR).
Abbreviations: SIAQ, self-injection assessment questionnaire; IQR, interquartile range.

The direct path coefficients of the model are presented in Table 4 and Figure 1. Compared with younger patients, older patients were more likely to experience lower self-confidence (β = −0.24; $P = 0.015$), self-image (β = −0.26; $P = 0.002$), and ease of use (β = −0.47; $P < 0.001$) after self-injection was completed. Female patients had lower ease of use than male patients (β = 0.17; $P = 0.036$). In terms of upper limb function, patients with greater difficulty in performing activities of daily living were more likely to have a lower self-image (β = 0.24; $P = 0.012$). Regarding the characteristics of the device, button-type self-injectors were associated with a higher satisfaction with self-injection (β = 0.24; $P = 0.006$).

Regarding the association between PRE and POST modules in the SIAQ, patients with better pre-feelings about injections had better post-feelings about injections (β = 0.81; $P < 0.001$), lower injection site reactions (β = 0.43; $P <$

Table 3 Pearson Correlation Coefficients Among the Self-Injection Assessment Questionnaire (SIAQ) Domains

	PRE Module			POST Module					
	1	2	3	4	5	6	7	8	9
Pre-feelings about injections (1)	1.00	0.09	0.15	0.74***	0.34**	0.42***	0.41***	0.34**	0.30**
Pre-self-confidence (2)		1.00	0.22*	0.01	0.03	0.32**	0.08	0.32**	0.19
Pre-satisfaction with medication (3)			1.00	0.05	0.01	0.04	0.17	0.12	0.19
Feelings about injections (4)				1.00	0.28*	0.34**	0.52***	0.48***	0.32**
Self-image (5)					1.00	0.23*	0.48***	0.23*	0.06
Self-confidence (6)						1.00	0.35**	0.42***	0.54***
Injection site reactions (7)							1.00	0.29**	0.40***
Ease of use (8)								1.00	0.46***
Satisfaction with self-injection (9)									1.00

Notes: The shading means correlation coefficients among the same module (PRE or POST module). *P<0.05, **P<0.01, ***P<0.001.

Table 4 Regression Weights Between Structural Parameters

		Unstandardized Direct Effects	Standardized Direct Effect	Standard Error	Critical Ratio	Significance Level
Self-confidence	← age	−0.03	−0.24	0.10	−2.44	0.015
Self-image	← age	−0.04	−0.26	0.08	−3.13	0.002
Ease of use	← age	−0.08	−0.47	0.07	−6.40	<0.001
Self-image	← sex	0.83	0.16	0.10	1.51	0.130
Ease of use	← sex	1.04	0.17	0.08	2.09	0.036
Self-image	← disability of upper limb function	0.26	0.24	0.10	2.51	0.012
Feeling about injections	← pre-feelings about injections	0.85	0.81	0.04	21.7	<0.001
Injection site reactions	← pre-feelings about injections	0.16	0.43	0.10	4.34	<0.001
Self-confidence	← pre-feelings about injections	0.36	0.42	0.10	4.12	<0.001
Self-image	← pre-feelings about injections	0.20	0.21	0.12	1.76	0.079
Ease of use	← pre-feelings about injections	0.42	0.41	0.10	4.25	<0.001
Self-confidence	← pre-self confidence	0.19	0.19	0.11	1.63	0.103
Satisfaction with self-injection	← pre-satisfaction with medication	0.16	0.17	0.09	1.82	0.069
Satisfaction with self-injection	← button-type self-injector	0.70	0.24	0.09	2.74	0.006
Satisfaction with self-injection	← injection site reactions	0.19	0.12	0.09	1.31	0.189
Satisfaction with self-injection	← self-confidence	0.26	0.35	0.09	4.07	<0.001
Satisfaction with self-injection	← ease of use	0.17	0.29	0.10	2.98	0.003

Notes: Unstandardized direct effects arise directly from the estimation procedure. Due to the metric differences of the instruments, standardized direct effects should be preferred to indicate the strength of the associations (magnitude between −1 and +1). Higher absolute values indicate a stronger (positive or negative) association. An absolute critical ratio >1.96 reflects that the path coefficients are significant at the 0.05 level.

0.001), higher self-confidence (β = 0.42; P < 0.001), and higher ease of use (β = 0.41; P < 0.001). Among the SIAQ POST modules, higher self-confidence (β = 0.35; P < 0.001) and ease of use (β = 0.29; P = 0.003) were associated with higher satisfaction with self-injection.

Discussion

This study showed that each patient's age, sex, and upper limb function as demographic and physical barriers as well as pre-feelings about injection as a psychological barrier were associated with patient experience with self-injection. These results suggest that patient training and education to focus on these factors are important in providing patients with greater confidence and empowerment in addition to increasing levels of independence, which may lead to improved rates of adherence to self-injection.[14]

Previous surveys on patient preference for the treatment mode of bDMARDs found that older patients with RA were more likely to prefer in-hospital dosing, whereas non-elderly adults were more likely to prefer self-administration.[4,15]

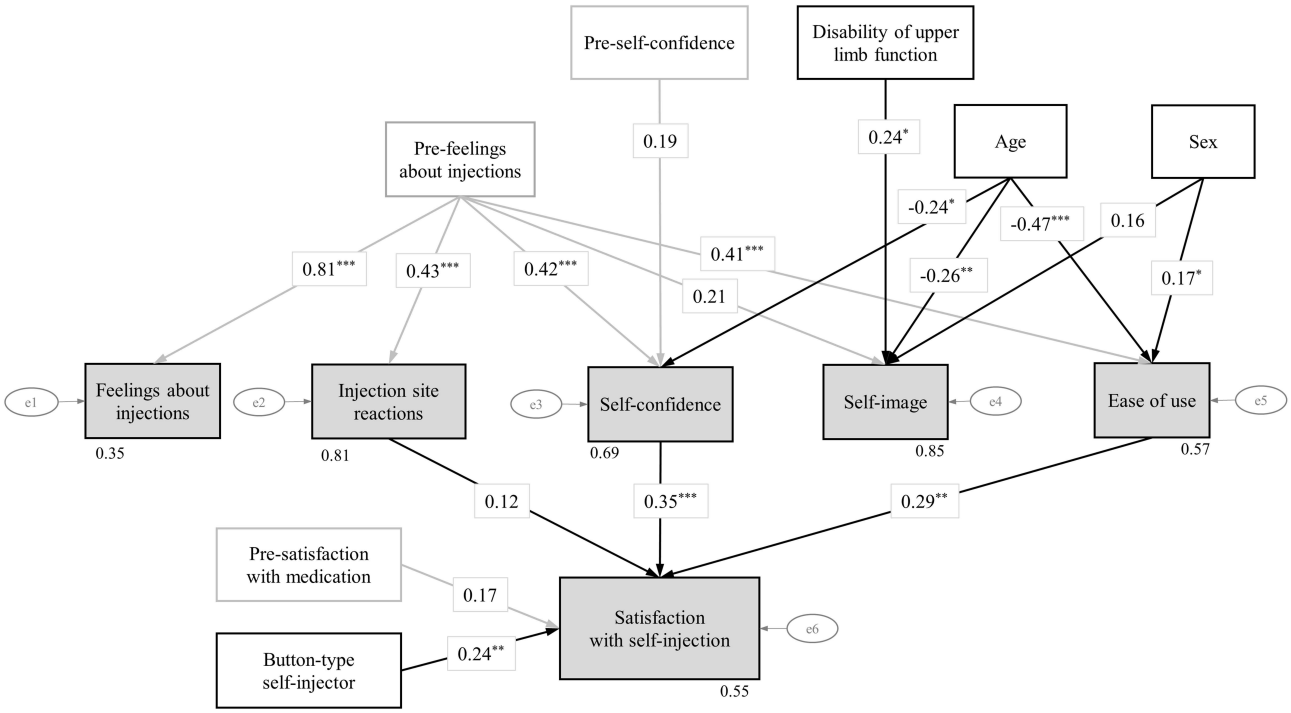

Figure 1 Estimated standardized direct effects for the proposed model. Squares represent measured variables (scale scores). Gray squares show the POST module of the Self-Injection Assessment Questionnaire, while white squares show the PRE module and other characteristics. Arrows connecting rectangles in one direction indicate a hypothesized direct relationship between the two variables. Circles in which the letter "e" is inscribed represent the associated error. *P<0.05, **P<0.01, ***P<0.001.

These studies did not examine why aging influenced preference for self-injection. Because our study showed that elderly patients were more likely to experience lower self-confidence, self-image, and ease of use, these factors may affect their preference for self-injection. In addition, elderly patients with RA is frequently associated with geriatric syndrome that make an elderly individual vulnerable to health or social challenges.[16] Geriatric syndrome consists of multiple and interrelated factors such as cognitive impairment, depression, fall, incontinence, sensory limitations and malnutrition. These impairments may be attributable to lower confidence, self-image, and ease of use in elderly patients with RA. One could therefore suggest that to assess and improve physical and mental impairments would help patient experience with self-injection in elderly RA patients.

A qualitative study showed that patients reported an alteration in perceived self-image following a diagnosis of RA.[17] In the present study, patients with severe disabilities of upper limb function or functional damage due to RA were more likely to have embarrassment associated with self-injection in public. Taken together, these results imply that RA treatment and care need to embrace not only physical difficulties but also the social and psychological components of care. Healthcare workers must acknowledge the physical aspects of RA and pay attention to their psychological and social consequences.

Feelings about injection before learning the method of self-injection, such as fear of needles and anxiety and fear of self-injection, were associated with several psychological perceptions and therefore, can be psychological barriers to self-injection. Previous studies have shown that negative concerns about self-injection include needle phobia; fear and anxiety; concerns about pain, stinging, and other injection site reactions; lack of confidence in correct administration; non-adherence to medications; and struggle to use a self-injection device.[8,14,18] However, the relationships among these factors were not examined. In this study, not only post-feelings about injections, but also self-confidence and ease of use were affected by pre-feelings about injection. Thus, an appropriate choice of device design and sufficient time to educate patients may enhance confidence and ease of correct self-injection directly[14] and indirectly through improvement of pre-feeling about injections. In addition, we identified that patients' anxiety and fear of self-injection influenced their subjective assessments of injection site reactions. Fernandez et al proposed three categories of injection site reactions:

(1) physical reactions due to needle and injection processes, (2) irritant reactions associated with the properties of the injected solution, and (3) allergic reactions, both immediate and delayed.[19] Because these biological reactions are subjectively assessed by patients, their psychological backgrounds may also affect the extent and frequency of injection site reactions. Healthcare workers should consider psychological backgrounds in assessing injection site reactions in an effort to relieve patients' anxiety and fear of self-injection, regardless of the severity of objective biological reactions.

Exploratory analysis showed that button-type self-injectors were directly associated with higher satisfaction with self-injection, without a mediating effect of ease of use. More active involvement in self-injection by pressing a button might increase self-efficacy, which leads to an increase in satisfaction.[20] However, there are several available device features, such as gripping area, audible sounds to help track the injection, needle not visible to patients, and automatic needle insertion.[14] These features may be confounded by the effect of button-type injections on satisfaction with self-injection. Further studies are needed to assess the effect of device design on patients' experiences with self-injection.

A strength of our study includes the assessment of detailed subjective patient experiences with self-injection. Several studies have suggested a gap between patients' confidence in their abilities and their actual competence to correctly self-inject, assessed by healthcare workers.[14,21] In one study, to gather feedback on injection experience, nurses reported higher levels of confidence regarding safe self-injection than the patients themselves reported. Thus, healthcare providers should also assess subjective patient experiences with self-injection to reassure patients and manage injection-related anxiety or uncertainty.

The present study has several limitations. First, the relatively small sample size may have influenced the robustness of the reported measurement characteristics and thus requires confirmation in larger cohorts, whereas the overall fit of the final measurement model was good, based on several goodness-of-fit indices. Second, the SIAQ domains might have been influenced by other factors such as level of education, cognitive function, and mental illness, which were not accounted for in the present study. However, a previous study showed that neurological and cognitive deficits, as well as fatigue, generally had no influence on ratings of satisfaction, functional reliability, or ease of use for self-injection among patients with multiple sclerosis.[22] Third, the sample size of this study was small. Because previous experience of self-injection may influence SIAQ score and present self-injectors cannot score the SIAQ PRE module, we limited patients who had no previous experience of self-injection or no experience for >1 year since the last self-injection. Although we consecutively recruited patients, the number of included patients was small, and therefore larger studies were needed. Lastly, recruitment was performed in a single center. Further research is required to determine whether the results can be generalized to different populations within these categories.

Conclusion

Demographic and physical barriers to patient experience with self-injection in patients with RA included older age, female sex, and worse upper limb function of patients, while psychological barriers included worse pre-feelings about injection. To optimize patients' experiences with self-injection, healthcare workers should assess these factors as potential demographic, physical, and psychological barriers. Because this study is mainly limited to patients with no previous experience of self-injection, future research is needed to examine the barriers to experience with self-injection in patients who currently self-inject.

Abbreviations

RA, rheumatoid arthritis; bDMARDs, Biological disease-modifying anti-rheumatic drugs; ACR, American College of Rheumatology; EULAR, European League Against Rheumatism; TNF, tumor necrosis factor; IL-6, interleukin-6; SIAQ, Self-Injection Assessment Questionnaire; CDAI, Clinical Disease Activity Index; HAQ, health assessment questionnaire; CFI, Comparative-of-Fit Index; TLI, Tucker-Lewis Index; RMSEA, root mean square error of approximation; SRMR, standardized root mean square residual.

Data Sharing Statement

The datasets generated and/or analysed during the current study are not publicly available due to patient's consent but are available from the corresponding author on reasonable request.

Ethics Approval and Informed Consent

The study was approved by the ethics committee of Kobe University Graduate School of Medicine (approval number: B210024) and conducted in accordance with the Declaration of Helsinki. The ethics committee waived the requirement for patients' informed consent because this study only utilized data collected in clinical practice including overall patient experience with subcutaneous self-injection and the opportunities to refuse inclusion into the research were ensured for the research subjects. The need for informed consent was waived by the ethics committee of Kobe University Graduate School of Medicine (approval number: B210024).

Acknowledgments

The abstract of this paper was presented at 24th Asia-Pacific League of Associations for Rheumatology (APLAR) Congress, 6–9 December 2022, Hong Kong as a poster presentation with interim findings. The poster's abstract was published in "Poster Abstracts" in International Journal of Rheumatic Diseases: https://doi.org/10.1111/1756-185X.14505. We would like to thank Editage for English language editing.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Funding

There is no funding to report.

Disclosure

AO reports grants from Pfizer Inc., Bristol-Myers Squibb., Ayumi, and Advantest, and personal fees from Asahi Kasei Pharma, Abbie Inc., Gilead Sciences Inc., Chugai Pharmaceutical Co., Ltd., Eli Lilly Japan K.K, Pfizer Inc., Bristol-Myers Squibb., Eisai, Janssen Pharmaceutical K.K., Mitsubishi Tanabe Pharma, Takeda Pharmaceutical Company Limited, and Daiichi Sankyo Co. Ltd. AO belongs to the department that is financially supported by five pharmaceutical companies (Tanabe-Mitsubishi, Chugai, Ayumi, UCB-Japan and Asahi-Kasei), Nagahama city and Toyooka city. JS reports grants from Asahi Kasei Pharma, AbbVie Inc., and Chugai Pharmaceutical Co., Ltd., and personal fees from Asahi Kasei Pharma, Abbie Inc., Chugai Pharmaceutical Co., Ltd., Eli Lilly Japan K.K, Pfizer Inc., Eisai, Janssen Pharmaceutical K.K., and Mitsubishi Tanabe Pharma. The remaining authors have no financial and non-financial conflicts of interest to disclose concerning this manuscript. The pharmaceutical companies had no role in the design of the study, the collection or analysis of the data, the writing of the manuscript, or the decision to submit the manuscript for publication.

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