Cluster analysis identifies the differential impact of disease activity and severity on functional status and patient satisfaction in rheumatoid arthritis: the FRANK registry

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Abstract

Objective

The purpose of the present study was to investigate the differential impact of disease activity and severity on functional status and patient satisfaction in rheumatoid arthritis (RA) using cluster analysis on data from the FRANK registry.

Methods

Data from 3,619 RA patients in the FRANK registry were analysed. Patients were grouped using hierarchical and k-means cluster analyses based on age, physician's global assessment (PhGA), patient's pain assessment (PtPA), and Steinbrocker stage. Clusters were evaluated for differences in functional status (mHAQ), quality of life (EQ5D), and patient satisfaction.

Results

Five distinct patient clusters were identified. In hierarchical cluster analysis, Cluster 1 (n=1195, 33.0%) and 2 (n=641, 17.7%) with lower disease activity and severity demonstrated better functional outcomes (mHAQ: 0.18±0.30 and 0.15±0.26, respectively) and higher satisfaction, with treatment efficacy scores of 1.9±0.7 and 2.0±0.7, respectively (1: very satisfied to 6: very unsatisfied). Cluster 3 (n=1117, 30.9%), characterised by less activity and more severity, showed significant joint damage (Steinbrocker stage III-IV: 95.4%) despite controlled inflammation. Cluster 4 (n=385, 10.6%), characterised by patient-physician discordance in disease activity (mean PhGA: 0.9±0.5; mean PtPA: 5.0±2.1), had a more pronounced negative effect on satisfaction. Cluster 5 (n=281, 7.8%), with more activity and moderate severity, had the poorest outcomes in functional status (mHAQ: 0.87±0.65), quality of life (EQ5D: 0.60±0.17), and satisfaction, with a treatment efficacy score of 2.9±0.9. k-Means clustering produced overall similar clusters to hierarchical clustering, allowing the same labels for Cluster 1 to Cluster 5.

Conclusion

The study highlights the importance of understanding the heterogeneous nature of RA and its impact on patient outcomes. Personalised treatment approaches that address both objective disease measures and subjective patient experiences are essential for optimising RA management. Identification of distinct patient phenotypes, particularly those in Clusters 3, 4, and 5, may guide tailored interventions to improve treatment satisfaction and long-term outcomes in RA.

Key words

rheumatoid arthritis, cluster analysis, disease progression, severity of illness index, patient satisfaction

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Introduction

The treat-to-target (T2T) strategy in managing rheumatoid arthritis (RA) aims to uphold a positive functional status and quality of life (QOL) by achieving long-term remission (1, 2), while also prioritising patient satisfaction with treatment (3, 4). This approach initially focuses on alleviating joint pain and swelling, key markers of disease activity, and subsequently on preventing the progression of joint destruction, indicative of disease severity (5). Both disease activity and severity significantly influence functional disability in both early and established RA stages (6). In Japanese patient cohorts, lower disease activity correlates with higher patient satisfaction (4), yet some residual symptoms may persist even after achieving clinical remission, impacting QOL (7).

Given the diverse patient backgrounds, including factors such as age, disease activity, and severity, the impact on functional status and satisfaction in RA may vary (6-8). Further exploration is essential to elucidate these distinct effects. Cluster analysis, an exploratory statistical method, offers a novel approach in real-world RA research by grouping data based on similarities (9-14). These data-driven methodologies have the potential to reveal previously unnoticed patterns within datasets, providing valuable insights for prognosis and treatment decisions.

This study utilised high-quality data from the FRANK registry, a regional observational cohort. By using indicators such as age, physician's global assessment (PhGA), and patient's pain assessment (PtPA) to gauge disease activity, alongside the Steinbrocker stage (SbS) as a measure of disease severity, we aimed to identify previously unrecognised patient phenotypes associated with disease activity and severity, and to clarify how these phenotypes may differentially impact functional status and patient satisfaction.

Materials and methods

Data collection

Data for this study were obtained from the Fukuoka Rheumatoid Arthritis Network (FRANK) Registry, conducted across 10 associated institutions since March 2018 (4). The FRANK Registry tracks the progression and management of RA patients over time. Clinical data were submitted to the data centre at Kyushu University Hospital through the Clinical Research Internet Network (CRIN-Q). Ethical approval for accessing and utilising the FRANK Registry data was obtained from the ethics committee at Kyushu University (approval no.: 29-277).

Enrolled patients were Japanese nationals over 18 years old, diagnosed with RA based on the 1987 American College of Rheumatology criteria (15). These patients were treated by rheumatologists following the guidelines of the Japan College of Rheumatology (16). Annually collected information included patient demographics (age, sex, body mass index), disease characteristics (duration and severity assessed through Steinbrocker stage), clinical assessments (visual analogue scale for PhGA, tender joints count, and swollen joints count), laboratory markers (CRP: C-reactive protein level; ESR: erythrocyte sedimentation rate), treatment modalities (medication usage, history of musculoskeletal surgeries), and comorbidities (cardiovascular disorders, osteoporosis). To gather additional insights into patient experiences and outcomes, participants completed self-administered questionnaires annually. These included pain VAS, general VAS, Modified Health Assessment Questionnaire (mHAQ) (17), EuroQol 5-Dimensional Questionnaire (EQ5D) (18), and patient satisfaction questionnaires. Satisfaction was assessed using a 6-point scale: very satisfied (1), satisfied (2), somewhat satisfied (3), somewhat unsatisfied (4), unsatisfied (5), and very unsatisfied (6). Satisfaction was further evaluated in four categories: 1. effect of treatment, 2. cost of treatment, 3. activities of daily living: ADL, and 4. global treatment. The questionnaires used in this study were validated in Japanese, the patients' native language. The validity of these questionnaires for data acquisition in this population has been confirmed in our previous research (4).

Cluster analysis

Between March 2018 and August 2023,

3,776 patients were continuously enrolled in the FRANK Registry. Of these, 3,619 individuals had complete data for the clustering variable candidates and were included in the analysis. The mean number of visits per patient was 3.1 (median 3), with a range of 1 to 6 visits depending on the time of entry into the registry. To account for the longitudinal nature of the registry and the varying number of visits per patient, we used the mean values of time-dependent clinical variables for each patient. This approach is consistent with the methodology used in a similar cluster analysis (9, 13). The distribution of the mean values for the time-dependent variables (PhGA, PtPA, CDAI: Clinical Disease Activity Index, SDAI: Simplified Disease Activity Index; Disease Activity Score: DAS28-CRP, DAS28-ESR, mHAQ, EQ5D, and patient satisfaction scores) was assessed using histograms and quantile-quantile plots. These variables generally followed a normal distribution, with right-skewness observed for PhGA, PtPA, CDAI, SDAI, and mHAQ.

The selection of clustering variables (age, PhGA, PtPA, and SbS) was based on their low intercorrelation, which is crucial for cluster analysis to identify distinct patient subgroups (Table I). The correlation matrix was used to assess the suitability of the selected variables for cluster analysis, ensuring that they were not highly correlated with each other, which could lead to redundancy in the clustering process. PhGA and PtPA had relatively lower correlation coefficients with each other compared to other disease activity indices such as CDAI, SDAI, DAS28-CRP, and DAS28-ESR. Hierarchical clustering (Ward's method) was the main clustering algorithm, with secondary analyses performed using k-means clustering with JMP software v. 14.2.0 (SAS Institute, Cary, NC, USA). The optimal number of clusters was determined as five based on the cubic clustering criterion (CCC) for different numbers of clusters (k=2 to k=10) (Table II). Cluster labels were assigned by examining the distributions of the cluster variables. Differences among the clusters for mHAQ, EQ5D, and patient satisfaction were described.

Table I. Pearson's correlation coefficients (r) for clustering variable candidates.

	Age	SbS	PhGA	PtPA	CDAI	SDAI	DAS28 (CRP)	DAS28 (ESR)
Age		0.15	0.09	0.03	0.06	0.08	0.11	0.23 *
SbS	0.15		0.20	0.12	0.18	0.18	0.18	0.19
PhGA	0.09	0.20		0.44 *	0.74 *	0.74 *	0.65 *	0.58 *
PtPA	0.03	0.12	0.44 *		0.57 *	0.57 *	0.55 *	0.47 *
CDAI	0.06	0.18	0.74 *	0.57 *		0.99 *	0.90 *	0.77 *
SDAI	0.08	0.18	0.74 *	0.57 *	0.99 *		0.93 *	0.78 *
DAS28 (CRP)	0.11	0.18	0.65 *	0.55 *	0.90 *	0.93 *		0.84 *
DAS28 (ESR)	0.23 *	0.19	0.58 *	0.47 *	0.77 *	0.78 *	0.84 *	

SbS: Steinblocker stage; PhGA: Physician's global assessment; PtPA: Patient's pain assessment; CDAI: Clinical Disease Activity Index; SDAI: Simplified Disease Activity Index; DAS28: Disease Activity Score 28. *$p<0.0001$.

Table II. Assessing the optimal number of clusters based on cubic clustering criterion.

Cluster number	2	3	4	5	6	7	8	9	10
Cubic clustering criterion	-10.3	-8.9	-18.3	3.4 optimal	0.5	0.8	-3.5	-4.9	-2.9

Statistical analysis

Differences in demographic, clinical, and patient-reported outcomes among the identified clusters were analysed using appropriate statistical methods. Continuous variables were compared using the Tukey-Kramer test, which accounts for multiple pairwise comparisons. Categorical variables were compared using Pearson's chi-square test. Statistical significance was set at $p<0.05$. All statistical analyses were conducted using JMP software v. 14.2.0 (SAS Institute, Cary, NC, USA).

Results

Hierarchical clustering revealed several distinct patient clusters based on disease activity and severity (Table III). The largest cluster, C1, comprising 1195 patients, exhibited lower PhGA, PtPA, and SbS, and was labelled 'less activity and less severity'. C2, with 641 patients, had similar characteristics but included younger individuals, earning the label 'less activity and less severity with lower age'. Conversely, C3, consisting of 1117 patients, demonstrated 'less activity and more severity', marked by higher SbS alongside lower PhGA and PtPA. C4, housing 385 patients, depicted 'patient-physician discordance in disease activity', featuring higher PtPA but lower PhGA and SbS. Finally, C5, the smallest cluster with 281 patients, was termed 'more activity and moderate severity', showcasing higher PhGA and PtPA but intermediate SbS levels.

k-Means clustering produced overall similar clusters to hierarchical clustering (Table III), allowing the same labels for C1–C5. The cluster sizes remained consistent, with 1242 individuals in C1, 784 in C2, 898 in C3, 255 in C4, and 440 in C5 (Table IV).

Disease duration was longest in Cluster 3 (mean 20.5 and 20.6 years in hierarchical and k-means clustering, respectively) and shortest in Clusters 2. Tender joint count, swollen joint count, CRP, ESR, CDAI, SDAI, DAS28-CRP, and DAS28-ESR, were highest in Cluster 5 and lowest in Clusters 1 and 2. Cluster 4 exhibited a higher mean tender joint count (4.1 and 4.8 in hierarchical and k-means clustering, respectively) relative to the mean swollen joint count (1.8 and 2.5, respectively). The use of bDMARDs or tsDMARDs was most prevalent in Cluster 3 (49.2% and 46.8%, respectively). The use of steroid was highest in Cluster 5 (68.0% and 70.2%, respectively) and lowest in Cluster 2 (30.7% and 31.6%, respectively).

Table V shows the comparison of mHAQ, EQ5D, and patient satisfaction based on hierarchical and k-means clustering. Clusters 1 and 2 collectively represented half of the total sample and exhibited favourable mHAQ, EQ5D, and satisfaction. Notably, Cluster 2,

Table III. Clustering by age, physician's global assessment (PhGA) and patient's pain assessment (PtPA), and Steinblocker stage.

	hierarchical clustering						k-means clustering					
	C1	C2	C3	C4	C5	Tukey-Kramer test or chi-square test	C1	C2	C3	C4	C5	Tukey-Kramer tes or chi-square test
Number of patients	1195	641	1117	385	281		1242	784	898	440	255	
Age	67.7 (8.2)	44.8 (9.7)	64.4 (11.8)	64.7 (14.7)	66.0 (12.5)	2 < 3, 4, 5 < 1	69.2 (7.4)	43.7 (9.0)	66.4 (9.4)	64.7 (12.1)	65.6 (12.8)	2 < 3, 4, 5 < 1
PhGA	0.5 (0.5)	0.7 (0.7)	1.0 (0.8)	0.9 (0.5)	4.1 (1.6)	1 < 2 < 3, 4 < 5	0.6 (0.6)	0.6 (0.7)	0.9 (0.7)	1.2 (0.5)	4.3 (1.5)	1, 2 < 3 < 4 < 5
PtPA	0.9 (0.9)	1.4 (1.3)	2.2 (2.2)	5.0 (2.1)	4.4 (2.3)	1 < 2 < 3 < 5 <4	1.0 (1.0)	1.4 (1.4)	1.5 (1.3)	6.1 (1.4)	4.6 (2.3)	1 < 2, 3 < 5 <4
Steinblocker Stage	1.7 (0.5)	1.4 (0.5)	3.6 (0.5)	1.4 (0.5)	2.5 (1.1)	2, 4 < 1 < 5 < 3	1.5 (0.5)	1.7 (0.8)	3.7 (0.5)	2.2 (1.1)	2.8 (1.0)	1 < 2 < 4 < 5 < 3
Gender (F/M)	875/318	547/92	974/136	296/87	226/55	p < 0.0001	887/355	680/104	786/112	356/84	209/46	p < 0.0001
Disease duration (years)	8.5 (8.6)	6.4 (6.9)	20.5 (12.2)	6.9 (8.6)	15.5 (13.2)	2, 4 < 1 <5 <3	8.1 (8.6)	7.7 (7.6)	20.6 (12.1)	11.6 (11.8)	17.8 (14.3)	1, 2 < 4 <5 <3
Tender joints (n.)	1.2 (3.9)	1.6 (4.1)	2.4 (4.8)	4.1 (6.7)	6.8 (10.4)	1, 2 < 3 < 4 < 5	1.4 (4.2)	1.5 (3.8)	1.8 (3.3)	4.8 (7.4)	7.3 (11.2)	1, 2, 3 < 4 < 5
Swollen joints (n.)	0.8 (2.1)	1.0 (2.6)	1.9 (3.3)	1.8 (3.8)	4.7 (5.9)	1, 2 < 3, 4 < 5	0.7 (1.9)	1.0 (2.6)	1.6 (2.8)	2.5 (4.3)	5.4 (6.6)	1, 2 < 3 < 4 < 5
CRP (mg/L)	2.9 (8.1)	2.6 (8.1)	3.9 (9.2)	4.9 (10.5)	9.4 (14.3)	1, 2 < 3, 4 < 5	3.0 (8.2)	2.4 (7.5)	3.5 (7.1)	5.7 (13.5)	10.4 (15.0)	1, 2, 3 < 4 < 5
ESR (mm/hr)	20.0 (17.8)	14.3 (13.8)	23.5 (21.4)	23.5 (19.7)	35.4 (25.8)	2 < 1 < 3, 4 < 5	20.5 (18.0)	13.9 (12.7)	23.6 (21.0)	25.5 (22.6)	37.1 (26.5)	2 < 1 < 3, 4 < 5
CDAI	2.7 (2.5)	2.9 (3.1)	4.3 (3.8)	5.4 (4.0)	12.5 (6.5)	1 < 2 < 3 < 4 <5	2.5 (2.6)	2.7 (3.1)	3.6 (2.8)	7.0 (4.3)	13.6 (7.0)	1, 2 < 3 < 4 <5
SDAI	2.6 (2.6)	3.1 (3.2)	4.7 (4.0)	5.9 (4.2)	13.5 (7.1)	1, 2 < 3 < 4 < 5	2.8 (2.8)	2.9 (3.2)	4.0 (3.0)	7.5 (4.5)	14.2 (7.5)	1, 2 < 3 < 4 < 5
DAS28 CRP	1.7 (0.5)	1.7 (0.6)	2.0 (0.7)	2.2 (0.7)	3.1 (0.9)	1, 2 < 3 < 4 < 5	1.7 (0.5)	1.7 (0.6)	1.9 (0.6)	2.4 (0.7)	3.1 (0.9)	1, 2 < 3 < 4 < 5
DAS28 ESR	2.2 (0.7)	2.1 (0.8)	2.6 (0.9)	2.8 (0.8)	3.8 (1.0)	1, 2 < 3 < 4 < 5	2.3 (0.7)	2.0 (0.8)	2.5 (0.8)	3.1 (0.9)	3.9 (1.1)	1, 2 < 3 < 4 < 5
Steinblocker class	1.2 (0.4)	1.2 (0.4)	1.8 (0.7)	1.4 (0.5)	2.0 (0.8)	1, 2 < 4 < 3 < 5	1.2 (0.4)	1.2 (0.4)	1.7 (0.6)	1.6 (0.7)	2.1 (0.8)	1, 2 < 4 < 3 < 5
Use of bDMARD or tsDMARD	334 (28.0%)	227 (35.4%)	549 (49.2%)	99 (25.8%)	107 (38.1%)	p < 0.0001	320 (25.8%)	306 (39.0%)	420 (46.8%)	168 (38.3%)	102 (40.0%)	p < 0.0001
Use of steroid	410 (34.3%)	197 (30.7%)	565 (50.6%)	187 (48.7%)	191 (68.0%)	p < 0.0001	446 (35.9%)	248 (31.6%)	440 (49.0%)	237 (54.0%)	179 (70.2%)	p < 0.0001

PhGA: Physician's global assessment; PtPA: Patient's pain assessment; CRP: C-reactive protein level; ESR: erythrocyte sedimentation rate; CDAI: Clinical Disease Activity Index; SDAI: Simplified Disease Activity Index; DAS28: Disease Activity Score 28.

which comprised younger individuals, showed lower satisfaction regarding costs compared to Cluster 1. Conversely, despite being the smallest, Cluster 5 demonstrated the poorest mHAQ, EQ5D, and satisfaction. Cluster 4, characterised by highest PtPA, ranked next least favourable, with a more pronounced negative effect on satisfaction compared to Cluster 3, although QOL remained consistent.

Discussion

This study utilised cluster analysis to explore the heterogeneous nature of RA and its impact on functional status and patient satisfaction within a large, multicentre cohort from the FRANK registry. By identifying five distinct patient clusters based on age, disease activity, and severity, we demonstrated that lower disease activity and severity are associated with better functional outcomes and higher satisfaction, particularly in Clusters 1 and 2. These clusters, representing patients with less active and less severe disease, emphasise the importance of achieving and maintaining low disease activity for optimal patient-reported outcomes (19).

Table IV. Cluster reclassification across five clusters between hierarchical clustering and k-means clustering.

		hierarchical clustering					
		C1	**C2**	**C3**	**C4**	**C5**	**SUM**
k-means clustering	**C1**	1031	63	7	115	26	1242
	C2	116	554	78	30	6	784
	C3	40	0	854	0	4	898
	C4	8	23	147	240	22	440
	C5	0	1	31	0	223	255
	SUM	1195	641	1117	385	281	3619

Our study carefully selected age, PhGA, PtPA, and SbS as clustering variables based on their low intercorrelation and ability to capture different aspects of RA heterogeneity (Table I). While composite indices like DAS28 CRP are widely used, we chose to use PhGA and PtPA separately to identify potential patient-physician discordance in disease activity assessment, as exemplified by cluster 4. This approach, combined with the validation of our findings using both hierarchical and k-means clustering methods, enhances the robustness and clinical relevance of the identified patient subgroups. Extended research could explore the impact of incorporating additional variables on clustering patterns, but our study demonstrates the value of selecting variables based on their intercorrelation and clinical significance, and validating the results using multiple clustering techniques.

The heterogeneity within RA patient populations necessitates personalised treatment approaches (20, 21). Clusters 4 and 5 revealed significant chal-

Table V. Comparison of mHAQ, EQ5D, and patient satisfaction based on hierarchical clustering and k-means clustering.

	hierarchical clustering						k-means clustering					
	C1	C2	C3	C4	C5	Tukey-Kramer test	C1	C2	C3	C4	C5	Tukey-Kramer test
mHAQ	0.18 (0.30)	0.15 (0.26)	0.53 (0.57)	0.48 (0.50)	0.87 (0.65)	1, 2 < 3, 4 < 5	0.19 (0.31)	0.15 (0.25)	0.47 (0.51)	0.69 (0.63)	0.95 (0.65)	1, 2 < 3 < 4 < 5
EQ5D	0.83 (0.13)	0.81 (0.12)	0.72 (0.16)	0.69 (0.13)	0.60 (0.17)	1, 2 < 3 < 4 < 5	0.82 (0.13)	0.82 (0.12)	0.74 (0.15)	0.65 (0.16)	0.58 (0.16)	1, 2 < 3 < 4 < 5
Patient satisfaction												
Efficacy	1.91 (0.66)	2.00 (0.71)	2.17 (0.73)	2.52 (0.81)	2.90 (0.94)	1, 2 < 3 < 4 < 5	1.94 (0.67)	1.99 (0.72)	2.11 (0.68)	2.65 (0.82)	2.93 (0.92)	1, 2 < 3 < 4 < 5
Cost	2.56 (0.94)	2.93 (1.06)	2.64 (1.10)	2.84 (0.94)	2.89 (1.21)	1, 3 < 2, 4, 5	2.54 (0.91)	2.96 (1.09)	2.60 (1.06)	2.83 (1.04)	2.87 (1.20)	1, 3 < 2, 4, 5
ADL	2.11 (0.70)	2.18 (0.81)	2.60 (0.90)	2.89 (0.82)	3.34 (0.97)	1, 2 < 3 < 4 < 5	2.16 (0.72)	2.16 (0.81)	2.51 (0.83)	3.09 (0.85)	3.43 (0.98)	1, 2 < 3 < 4 < 5

mHAQ: modified Health Assessment Questionnaire; EQ5D: EuroQol 5-Dimensional Questionnaire; ADL: activities of daily living.

lenges, with Cluster 5, characterised by higher disease activity and moderate severity, experiencing the poorest outcomes in terms of mHAQ, EQ5D, and patient satisfaction. In contrast, Cluster 4, which exhibited patient-physician discordance in disease activity (high PtPA but low PhGA and SbS), exhibited a distinct pattern of joint involvement with higher mean tender joint count (4.1) relative to the mean swollen joint count (1.8). This disparity may suggest the influence of factors beyond overt inflammation and deformity, such as central sensitisation or comorbid conditions like fibromyalgia. While we did not specifically assess fibromyalgia, the clinical profile of Cluster 4 is consistent with the findings reported by Kannayiram *et al*. (22), where elevated DAS28-ESR scores in RA patients with comorbid fibromyalgia were associated more with tender joint counts. However, diagnosing fibromyalgia in RA can be challenging (23, 24), and future studies incorporating specific fibromyalgia assessments would help clarify its prevalence and impact in subgroups like Cluster 4. The identification of patient-physician discordance underscores the importance of considering both objective measures and patient-reported outcomes in managing RA, tailoring treatment approaches to address the unique needs of this subgroup.

Understanding patient satisfaction in real-world heterogeneous RA cohorts is crucial, as it significantly influences treatment adherence and continuation (4, 25, 26). Our study uncovered specific patterns of satisfaction and dissatisfaction across different patient phenotypes using data-driven clustering. For instance, younger patients in Cluster 2, despite having lower disease activity and severity, reported lower satisfaction regarding treatment costs compared to older patients in Cluster 1. This finding indicates that economic factors are significant and should be addressed, particularly for younger RA patients who may face financial constraints impacting their overall treatment experience (27, 28).

Cluster 3 represents a distinct group within the RA patient population, characterised by lower disease activity but higher disease severity, indicating significant joint damage despite controlled inflammation. These patients typically experience substantial functional impairment due to advanced joint destruction, highlighting the critical need for interventions targeting joint health beyond inflammation control. While their functional outcomes and quality of life (mHAQ and EQ5D) were better than those in Cluster 5, they remained suboptimal compared to Clusters 1 and 2. This suggests that ongoing physical limitations from severe joint damage significantly impact their daily lives and satisfaction with treatment. Effective management for Cluster 3 patients should include not only maintaining low disease activity but also addressing severe joint damage through orthopaedic surgeries, rehabilitation programmes, and comprehensive pain management strategies (29, 30).

This study has several limitations that should be considered when interpreting the findings. First, the data were derived from the FRANK registry, which, while comprehensive, may not be entirely representative of the broader RA patient population due to its regional focus in Japan. This geographic limitation could affect the generalisability of the results to other populations with different demographic and clinical characteristics. Second, the study relied on self-reported measures for patient satisfaction and quality of life, which are inherently subjective and may be influenced by factors not directly related to disease activity or severity, such as personal expectations and socio-economic status. Additionally, the clustering variables were limited to age, PhGA, PtPA, and SbS, and did not include other potentially relevant factors such as genetic markers, specific treatment regimens, or detailed comorbidity profiles, which might provide a more comprehensive understanding of patient phenotypes. Furthermore, our study did not include specific assessments of fatigue, dietary habits, physical activity levels, or sleep disturbances, which are known to impact disease activity, functional status, and overall well-being in RA patients (12, 31-34). Future studies should aim to incorporate a broader range of variables and longitudinal data to validate these findings and explore the dynamic nature of RA and its impact on patient outcomes.

Conclusion

This study underscores the importance of understanding the differential impacts of disease activity and severity on functional status and patient satisfaction in RA. Cluster analysis revealed distinct patient phenotypes within the RA population, highlighting the need for personalised treatment approaches to optimise outcomes. By addressing both objective disease measures and subjective patient experiences, healthcare providers can enhance the overall treatment experience for RA patients, ultimately improving adherence and long-term outcomes.

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