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Health-related quality of life in patients with immune mediated inflammatory diseases: A cross-sectional, multidisciplinary study

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ABSTRACT

Immune mediated inflammatory diseases (IMIDs) have similarities in pathophysiology and treatment. Not much is known, however, about health-related quality of life (HR-QoL) in IMIDs. We assessed and compared HR-QoL, using the validated EuroQoL 5-dimensions 5-levels questionnaire, in an observational cohort comprising 530 patients (67.5% female, mean age 49 years (95% CI 35.9–50.9), mean disease duration 31.0 months (95% CI 27.2–34.8)), with the following IMIDs: connective tissue diseases (32.6%), uveitis (20.8%), inflammatory arthritis (17.7%), psoriasis (15.5%), vasculitis (6.2%), primary antiphospholipid syndrome (4.2%), and autoinflammatory diseases (2.8%). Patients used either no anti-inflammatory therapy (31.5%), monotherapy (28.7%), or a combination of anti-inflammatory drugs (39.8%). The mean HR-QoL utility score was 0.75 (95% CI 0.72–0.78). Multinominal logistic regression analysis showed a statistically significant association between a very low HR-QoL (utility score (< 0.70)) and female sex, rheumatological IMID or psoriasis, smoking or having smoked in the past, and current biological disease modifying anti-rheumatic drugs use.

1. Introduction

Immune mediated inflammatory diseases (IMIDs) can induce organ damage, physical disability, and impair work-related productivity [1,2]. Importantly, IMIDs are not uncommon: the overall prevalence of this group of diseases has been estimated to affect 5–7% of the population in Europe and the United States [3]. Because IMIDs share common immune pathogenic mechanisms, they are often treated with the same medication.

In the last decades, treatment options for IMIDs have dramatically improved [3,4]. Conventional disease modifying anti-rheumatic drugs (cDMARDs), as mono- or combination therapy, became the cornerstone of the treatment of many IMIDs. Additionally, initiation of treatment in the early stage of the disease and tight control are now key elements in the management of rheumatic conditions [5]. With the introduction of biological DMARDs (bDMARDs), which target specific aspects of the immune system, there is now a broad repertoire of anti-inflammatory treatments available for patients with IMIDs.

Although modern treatment strategies led to improvement of outcomes in IMIDs, such as the degree of inflammation and damage in different organ systems, health-related quality of life (HR-QoL) is often still compromised in patients with IMIDs. Multiple studies have evaluated the HR-QoL in individual IMIDs [6–8]. However, not much is known about HR-QoL differences between different IMIDs that were compared directly to one another in the same setting and using the same methods. Yet, HR-QoL is important when understanding the impact of disease on a patient's life and indirectly evaluating quality of provided care.

There are different ways to assess HR-QoL. The EuroQoL 5-dimensions 5-levels (EQ-5D-5 L) is a generic questionnaire validated for the assessment

Abbreviations: APS, antiphospholipid syndrome; BMI, Body mass index; bDMARD, biological disease modifying anti-rheumatic drug; cDMARD, conventional disease modifying anti-rheumatic drug; CI, confidence interval; CRP, C-reactive protein; eGFR, estimated glomerular filtration rate; EQ-5D-5 L, EuroQoL 5-dimensions 5-levels; ESR, erythrocyte sedimentation rate; HbA1c, hemoglobin A1c; HDL, high density lipoprotein; HR-QoL, health-related quality of life; IMID, Immune mediated inflammatory disease; LDL, low density lipoprotein; MCID, minimal clinical important difference; RA, rheumatoid arthritis; SF-36, Short Form-36.; SLE, systemic lupus erythematosus; VAS, visual analogue scale

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of HR-QoL and for economic analyses in the Netherlands [9]. It covers five dimensions: mobility, self-care, usual activity, pain and discomfort, and anxiety and depression. The Short Form-36 (SF-36) is a 36-item patient-reported survey measuring health status in eight domains (vitality, physical functioning, pain, physical, emotional and social functioning and mental health) [10].

The main goal of this study was to assess and compare HR-QoL scores with EQ-5D-5 L in patients with IMIDs across different departments in the University Medical Center Utrecht, Utrecht, The Netherlands, and to identify determinants of reduced HR-QoL.

2. Methods

We conducted a cross-sectional analysis of baseline data from an ongoing prospective cohort study (U-I&I) embedded in routine health care to collect data on cardiovascular risk factors and quality of life of patients with IMIDs.

2.1. Patients

All newly referred patients with existing or new-onset chronic IMIDs visiting the outpatient clinics of the departments of Rheumatology and Clinical immunology (henceforth referred to as Rheumatology), Ophthalmology, and Dermatology at the University Medical Center Utrecht were eligible for inclusion. The University Medical Center Utrecht serves as a tertiary referral hospital for chronic IMIDs, and patients were referred by either first-line care providers in the province of Utrecht or by medical specialists in second-line regional hospitals across the Netherlands. The most common reasons for referral included requests for a second opinion related to diagnosis or treatment, a medical indication for a complex therapeutic regimen, or the patient's own preference. Most of the newly referred patients who already had a diagnosis were previously diagnosed in a second-line regional hospital.

The Rheumatology department enrolled patients with any chronic IMID as well as patients already enrolled in a linked cohort study on systemic lupus erythematosus (SLE). The Ophthalmology department enrolled patients diagnosed with uveitis and the Dermatology department patients with psoriasis. Patients were enrolled by their own physician, and all physicians working in the three participating departments enrolled patients. All patients included in this analysis provided informed consent. The analyses presented in this paper used linked anonymized routine health care data only.

2.2. Data collection

The data collection consisted of routine health care data extracted from the hospital's electronic patient record system (Health care Information Exchange, Chipsoft, Amsterdam, Netherlands) using enterprise data warehouse (Summa Data Solutions Raamsdonkveer, the Netherlands) with SAS software (Version 9.4, Copyright © 2013 SAS Institute Inc). In this paper, only data extracted from each patient's first hospital visit was used, but in the ongoing cohort, data is extracted from each patient record annually.

Some components of the routine data collection were standardized whereas others were personalized based on the patient's medical history, diagnosis, and current health status. The standardized data included age, gender, lifestyle characteristics, diagnosis, anthropometric measures, a mandatory set of laboratory assessments, and the EQ-5D-5 L questionnaire. Lifestyle characteristics were recorded in the electronic patient record by nurses. Physicians' diagnoses were in accordance with the International Statistical Classification of Diseases and Related Health Problems (10th revision, ICD-10). Anthropometric measures were also assessed by a physician and included weight, height, pulse, and systolic and diastolic blood pressure. Body mass index (BMI) was derived by dividing the weight in kilograms by the square of the height in meters. The mandatory set of laboratory assessments included kidney function (plasma creatinine and estimated glomerular filtration rate (eGFR)), hemoglobin A1c (HbA1c), hemoglobin, and objective markers of inflammation (C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR)). Comorbidities were assessed using the age-adjusted Modified Charlson Comorbidity Index (mCCI) [11]. This index was calculated by the sum of physician and patient reported comorbid conditions: diabetes mellitus, chronic obstructive pulmonary disease (COPD), myocardial infarction, congestive heart failure, peripheral vascular disease, cerebrovascular disease, peptic ulcer disease, dementia, kidney disease, leukemia, lymphoma, solid-tumor cancer, liver disease, hemiplegia and AIDS. Age-adjustment was done adding one point for every decade age 50 years and over, with a maximum of four points. The maximum score is 38 points.

Each patient received an invitation to complete the EQ-5D-5 L questionnaire online after the hospital visit by automated email [12]. Patients completed the questionnaire within a mean of 12 days after the invitation was sent. Each completed questionnaire was automatically stored in the electronic patient record. The patient scored each dimension from 1 to 5 (1 = no problem, 2 = slight problem, 3 = some problem, 4 = moderate problem, 5 = extreme problem). The five dimensional scores were subsequently used to calculate one overall utility score, which ranges from 0 (worst) to 1 (best; no problems in any of the dimensions) [13]. The questionnaire also includes a 20 cm visual analogue scale (VAS) that patients used to self-rate their current overall health status. Studies have shown that the minimal clinical important difference (MCID) of the EQ-5D-5 L utility score and VAS are 0.08 and 10 points, respectively [14]. This threshold value of change in score can be used to interpret the significance of results from a clinical point of view.

The personalized data that was extracted from the electronic patient file after the hospital visit had been completed included referral information, disease duration, and medication use, all of which were recorded by a physician. We defined disease duration as the number of months between the visit date and the month and year in which the patient was diagnosed. The medication data in the electronic patient files is routinely verified, and corrected if needed, by hospital pharmacy staff using a national electronic system in which all pharmacies in the Netherlands participate. We defined past treatment as a treatment received during a period of at least 6 weeks but discontinued prior to enrollment. We defined current treatment as a treatment that the patient received within 6 weeks after enrollment.

2.3. Data-analysis

We used descriptive statistics to summarize sociodemographic and clinical characteristics. The EQ-5D-5 L data were presented and analyzed as utility scores in a continuous manner as well as in categories (low <0.70, intermediate 0.70–0.85, and high >0.85). Pearson's Chi-square test and ANOVA were used to test for differences between groups in the case of categorical and continuous variables, respectively. Potential determinants of HR-QoL were selected a priori, and each of these were tested in bivariable multinomial logistic regression analysis with the HR-QoL utility score as a categorical outcome. Those that were statistically significantly associated with the outcome at $p < .05$ were added to a multivariable multinomial logistic regression model with the same outcome. Statistical analyses were performed using IBM SPSS version 25 (IBM Corp., Armonk, NY, USA).

3. Results

3.1. Patient characteristics

The analyses included data from all 530 new patients who were enrolled in the three departments between 7 February 2017 (the start of the study) until 29 November 2018. Their mean age was 49 years (range 18–92) and 67.5% were women (Table 1). Patients were diagnosed with a connective tissue disease (32.6%), uveitis (without concomitant connective tissue disease) (20.8%), inflammatory arthritis (17.7%), psoriasis (15.5%), vasculitis (6.2%), primary antiphospholipid syndrome (APS) (4.2%), or an autoinflammatory disease (2.8%). Connective tissue diseases included mostly SLE (52.9% of those with connective tissue diseases), systemic sclerosis (18.4%),

Table 1
Patient characteristics: demographic, clinical, and laboratory parameters.

Characteristics	Total N=530	CTDs N=174	IA N=94	Vasculitis N=33	APS N=22	AI N=15	Uveitis N=110	Psoriasis N=82	p-value[1]
Age in years (mean, 95% CI)	49.0 (35.9-50.9)	49.0 (46.9-51.2)	42.9 (39.2- 46.6)	58.8 (53.7-63.9)	47.7 (43.3-52.2)	40.5 (30.6-50.3)	51.4 (48.5-54.3)	50.9 (47.6-54.1)	<.001
Female sex (n, %)	358 (67.5)	150 (86.2)	59 (62.8)	20 (60.6)	18 (81.8)	6 (40.0)	76 (69.1)	29 (35.4)	<.001
Department (n, %)									
- Rheumatology	358 (67.5)	174 (100.0)	93 (98.9)	32 (97.0)	22 (100.0)	15 (100.0)	5 (4.5)	17 (20.7)	<.001
- Ophthalmology	106 (20.0)	0	0	1 (3.0)	0	0	105 (95.5)	0	<.001
- Dermatology	66 (12.5)	0	1 (1.1)	0	0	0	0	65 (79.3)	<.001
Disease duration in months (mean, 95% CI)[2]	31.0 (27.2-34.8)	43.4 (35.9-50.9)	28.8 (21.3-36.2)	13.8 (3.5-24.0)	16.4 (1.1-31.8)	33.6 (8.0-59.2)	6.2 (1.6-10.8)	40.9 (32.0-49.9)	<.001
Smoking (n,%)									
- Never smoked	129 (39.0)	51 (42.5)	24 (40.7)	9 (34.6)	5 (33.3)	2 (20.0)	27 (40.9)	11 (31.4)	.213
- Past smoker	147 (44.4)	49 (40.8)	20 (33.9)	15 (57.7)	10 (66.7)	6 (60.0)	31 (47.0)	16 (45.7)	
- Smoker	55 (16.6)	20 (16.7)	15 (25.4)	2 (7.7)	0 (0)	2 (20.0)	8 (12.1)	8 (22.9)	
Alcohol use (n, %)									
- Never	77 (23.5)	24 (20.5)	13 (22.4)	8 (30.8)	2 (13.3)	3 (30.0)	20 (30.3)	7 (20.0)	.747
- Past	49 (15.0)	18 (15.4)	10 (17.2)	5 (19.2)	4 (26.7)	2 (20.0)	6 (9.1)	4 (11.4)	
- Current	201 (61.5)	75 (64.1)	35 (60.3)	13 (50.0)	9 (60.0)	5 (50.0)	40 (60.6)	24 (68.6)	
BMI (mean, 95% CI)	26.2 (25.7-26.8)	25.0 (24.1-25.8)	25.4 (24.0-26.8)	27.8 (25.1-30.1)	24.9 (22.6-27.2)	24.4 (21.5-27.2)	26.5 (25.4-27.7)	28.5 (27.2-29.8)	<.001
Systolic BP (mean, 95% CI)	135 (130-140)	130 (126-133)	129 (125-134)	135 (130-140)	133 (120-141)	120 (108-132)	147 (124-170)	137 (133-141)	.307
Diastolic BP (mean, 95% CI)	82 (81-83)	80 (78-82)	82 (77-82)	78 (71-86)	87 (81-93)	74 (66-82)	86 (83-89)	85 (83-87)	< .001
CRP in mg/L (mean, 95% CI)	7.0 (5.1-9.0)	5.1 (3.7-6.6)	13.3 (4.2-22.3)	13.1 (4.1-22.2)	3.2 (1.1-5.3)	10.7 (0.2-21.2)	4.0 (2.4-5.6)	4.7 (3.3-6.2)	.023
< 10 mg/L	415 (78.3)	141 (89.2)	67 (77.9)	19 (63.3)	16 (88.9)	11 (73.3)	96 (92.2)	66 (86.8)	.037
≥ 10 mgl/L	70 (13.2)	17 (10.8)	19 (22.1)	11 (36.7)	2 (11.1)	4 (26.7)	7 (6.8)	10 (13.2)	
ESR in mm/h (mean, 95% CI)	12.1 (10.8-13.4)	13.0 (11.6-16.0)	14.3 (10.3-18.3)	18.3 (9.9-26.7)	12.1 (5.2-18.9)	10.9 (4.9-16.9)	8.3 (6.6-9.9)	7.6 (6.0-9.2)	<.001
< 20 mm/h	419 (79.1)	136 (79.1)	74 (84.1)	25 (78.1)	13 (86.7)	18 (85.7)	81 (93.1)	72 (93.5)	.020
≥ 20 mm/h	73 (13.7)	36 (20.9)	14 (15.9)	7 (21.9)	2 (13.3)	3 (14.4)	6 (6.9)	5 (6.5)	
Creatinine in umol/L (mean, 95% CI)	70.6 (68.1-73.2)	71.1 (64.4-77.8)	66.0 (63.4-68.5)	84.1 (71.0-97.2)	72.0 (67.9-76.1)	64.6 (59.2-70.0)	68.1 (65.3-70.9)	73.9 (70.8-77.0)	.069
HbA1c in mmol/L (mean, 95% CI)	36.6 (35.7-37.4)	34.6 (33.3-35.9)	35.1 (34.2-36.0)	40.1 (36.5-43.8)	34.0 (32.8-35.2)	37.4 (35.2-39.5)	37.1 (32.2-42.1)	40.1 (36.4-43.9)	<.001
Current medication (n, %)[3,5]									
- None	162 (30.6)	49 (28.2)	7 (7.5)	6 (18.2)	13 (59.1)	4 (26.7)	55 (50.0)	28 (34.2)	< .001
- Monotherapy	129 (24.3)	34 (19.5)	27 (28.7)	5 (15.2)	8 (36.4)	3 (20.0)	29 (26.4)	23 (28.0)	
- Combination therapy	239 (45.1)	91 (52.3)	60 (63.8)	22 (66.7)	1 (4.5)	8 (53.3)	26 (23.6)	31 (37.8)	
Current monotherapy (n,%)[3,5]	N=129	N=34	N=27	N=5	N=8	N=3	N=29	N=23	
- NSAIDs	21 (16.3)	8 (23.5)	10 (37.1)	0	0	0	1 (3.4)	2 (8.7)	< .001
- Steroids[4]	47 (36.4)	8 (23.5)	3 (11.1)	3 (60.0)	0	1 (33.3)	26 (89.7)	6 (26.1)	
- cDMARDs	41 (31.8)	18 (52.9)	8 (29.6)	0	8 (100.0)	2 (66.7)	2 (6.9)	3 (13.0)	
- bDMARDs	20 (15.5)	0	6 (22.2)	2 (40.0)	0	0	0	12 (66.7)	
Current combination (n,%)[3,5]	N=239	N=96	N=60	N=22	N=1	N=8	N=26	N=31	< .001
- NSAID+steroid[4]	13 (5.4)	4 (4.4)	2 (3.3)	1 (4.5)	0	1 (12.5)	3 (11.5)	2 (6.5)	
- NSAID+cDMARD	25 (10.5)	9 (9.9)	13 (21,7)	0	1 (100)	0	0	2 (6.5)	
- NSAID+bDMARD	10 (4.2)	1 (1.1)	5 (8.3)	0	0	1 (12.5)	0	3 (9.7)	
- Steroid+cDMARD[4]	95 (39.7)	43 (47.3)	15 (25.0)	11 (50.0)	0	4 (50.022)	17 (65.4)	5 (16.1)	
- Steroid+bDMARD[4]	14 (5.9)	4 (4.4)	1 (1.7)	3 (13.6)	0	1 (12.5)	0	5 (16.1)	
- c+cDMARD	21 (8.8)	2 (2.2)	6 (10.0)	0	0	0	1 (3.8)	12 (38.7)	
- c+bDMARD	38 (15.9)	11 (12.1)	12 (20.0)	7 (31.8)	0	1 (12.5)	5 (19.2)	2 (6.5)	
- c+bDMARD+NSAID	22 (9.2)	17 (18.6)	5 (8.3)	0	0	0	0	0	
- c+bDMARD+ steroid[4]	1 (0.4)	0	1 (1.7)	0	0	0	0	0	
- Other therapies[7]	9 (3.8)	5 (5.5)	1 (1.7)	0	0	0	3 (11.5)	0	
Past medication use (n,%)[3,6]									
- None	290 (54.7)	71 (40.8)	45 (47.9)	19 (57.6)	18 (81.8)	7(46.7)	98 (89.1)	32 (40.8)	<.001
- NSAIDs	73 (13.8)	27 (15.5)	26 (27.7)	3 (9.1)	1 (4.5)	3 (20.0)	1 (1.0)	12 (16.4)	
- Topical steroids[4]	77 (14.5)	29 (16.7)	11 (11.7)	1 (3.0)	0 (0)	1 (6.7)	7 (6.4)	28 (34.1)	
- Oral or IV steroids[4]	127 (24.0)	70 (40.2)	19 (20.2)	12 (36.4)	1 (4.5)	6 (40.0)	6 (5.5)	12 (14.6)	
- cDMARDs	174 (32.8)	94 (54.0)	34 (36.2)	6 (18.2)	4 (18.2)	4 (26.7)	5 (4.5)	27 (32.9)	
- bDMARDs	3 (0.6)	13 (7.5)	17 (18.1)	1 (3.0)	0 (0)	2 (13.3)	2 (1.8)	28 (34.1)	

(*continued on next page*)

Table 1 (*continued*)

Modified Charlson Comorbidity Index (Mean, 95% CI)	1.2 (1.1-1.3)	1.0 (0.8-1.2)	1.7 (0.6-1.3)	2.0 (1.4-2.6)	0.9 (0.4-1.3)	0.7 (0.1-1.3)	1.6 (1.3-1.9)	1.2 (0.9-1.5)	<.001

AI, autoinflammatory conditions; APS, antiphospholipid syndrome; bDMARDs, biological disease modifiying antirheumatic drugs; BMI, body mass index; BP, blood pressure; cDMARDs, conventional disease modifiying antirheumatic drugs; CI, confidence interval; CRP,C-reactive protein (normal range 0-10 mg/dL); CTDs, connective tissue diseases; ESR, estimated sedimentation rate (normal range 0-20 mg/dL); HbA1c, Hemoglobulin A1c (normal range < 42); IV, intravenous; IA, inflammatory arthritis; NSAIDs, non-steroidal anti-inflammatory drugs.
1. We used ANOVA for means and Chi-squared for categorical variables.
2. Definition of disease duration: the number of months between the hospital visit and the month and year of diagnosis. There were 105 missing values, for all other valuables, missing values <10.
3. Medication to target the inflammatory process was included.
4. In the table, all patients that were stated to use steroids, used topical, oral or intravenous corticosteroids.
5. Current medication use was defined as medications initiated within 6 weeks following inclusion.
6. Medication history was defined as medications received for a period of at least 6 weeks but discontinued prior to inclusion. Patients could either use no therapy, monotherapy or combination therapy.
7. Other medication combinations: immunoglobulins intravenous or autologous stem cell transplantation.

and Sjogren's syndrome (16.1%), but also mixed connective tissue diseases (6.9%) and inflammatory myopathies (4.0%). Inflammatory arthritis included mostly rheumatoid arthritis (RA) (47.9% of those with inflammatory arthritis), but also ankylosing spondylitis (16.0%), psoriatic arthritis (15.9%), and juvenile idiopathic arthritis (12.8%). Of all patients, 10.9% (n = 63) received care in all three departments, 16.0% in the Rheumatology and Dermatology departments, 14.3% in the Rheumatology and Ophthalmology departments, and 0.5% in the Dermatology and Ophthalmology departments, over the past five years (Fig. 1).

The majority of participants were current (16.6%) or past smokers (44.4%). The mean number of pack years reported by current and past smokers combined was 13 years (95% confidence interval (CI) 11–15 years). Overall mean BMI was 26.2 (95% CI 25.7–26.8). Patients enrolled by the dermatology department had a significantly higher BMI (28.0) compared to patients enrolled by the ophthalmology (26.8) and rheumatology departments (25.6) (p < .01). Mean systolic blood pressure was 135 mmHg (95% CI 130–140) and mean diastolic blood pressure was 82 mmHg (95% CI 81–83). Patients with uveitis had a significantly higher mean systolic blood pressure (147 mmHg) than the other IMID patients (p = .04).

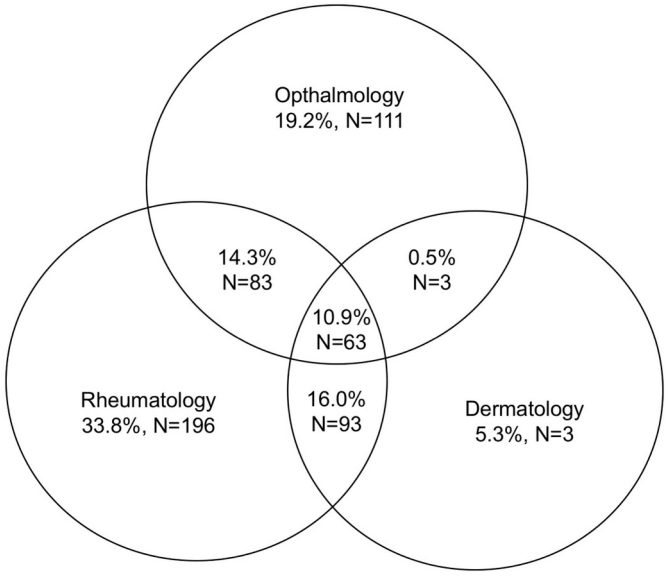

Fig. 1. Overview of patient appointments in the three departments over the last five years (in 530.
patients).

3.2. Medication use

At the time of the hospital visits, patients were either on monotherapy (24.3%), combination therapy (45.1%), or no therapy (30.6%). Current monotherapies comprised of NSAIDs (16.3%), corticosteroids (36.4%), cDMARDs (31.8%), or bDMARDs (15.5%) (Table 1). Medication use differed across the departments. cDMARDs (as part of either monotherapy or combination therapy) were currently used by 45.5%, 17.0%, and 9.1% of patients in the departments of Rheumatology, Ophthalmology, and Dermatology, respectively, and bDMARDs by 17.0%, 2.8% and 45.5%, respectively.

3.3. Comorbidity

The mean mCCI was 1.2 (95% confidence interval (CI) 1.1–1.3). Patients with APS and autoinflammatory disease had the lowest mean index (0.90, 95% confidence interval (CI) 0.4–1.3 and 0.70, 95% confidence interval (CI) 0.1–1.3, respectively). Patients with vasculitis had the highest mean mCCI 2.0, 95% confidence interval (CI) 1.4–2.6). Cancer (N = 36) and diabetes mellitus (N = 33) were most frequently reported comorbidities. Patients with uveitis had more often a diagnosis of cancer (N = 16, 14.5%, p = .02) compared with the other diagnoses. There were no other significant differences between the other comorbid conditions.

3.4. HR-QoL

All patients combined had a mean EQ-5D-5 L utility score of 0.75 (95% CI 0.72–0.78) (Table 3). When divided in the three categories, 36.5% had a high (>0.85), 36.8% an intermediate (0.70–0.85), and 26.7% a low utility score (<0.70). Patients with inflammatory arthritis had the lowest (0.71, 95% CI 0.66–0.76) and patients with uveitis the highest mean utility score (0.85, 95% CI 0.80–0.90). The mean current health status VAS score was 68.8 (95% CI 66.7–70.9), and this score was lowest in vasculitis patients (59.2, 95% CI 50.0–68.4) and highest in uveitis patients (77.8, 95% CI 73.3–82.3). The EuroQol subdomains mobility, selfcare and usual care were also significantly different between IMIDs (see Table 2). Patients with vasculitis scored significantly higher, meaning more impairment, on the domain usual activities and anxiety and depression compared to the other IMIDs. In the mobility domain, patients with autoinflammatory diseases and inflammatory arthritis had a significantly higher score. Patients with uveitis had the lowest scores in all domains.

Table 2
HR-QoL scores across different IMIDs.

Characteristics	Total N=307	CTDs N=174	IA N=94	Vasculitis N=33	APS N=22	AI N=15	Uveitis N=110	Psoriasis N=82	p-value[1]
Euroqol utility score[2] (mean, 95% CI)	0.75 (0.72-0.78)	0.75 (0.71-0.79)	0.71 (0.66-0.76)	0.72 (0.64-0.79)	0.80 (0.70-0.90)	0.78 (0.70-0.86)	0.85 (0.80-0.90)	0.72 (0.63-0.80)	.042
Euroqol utility score[2] categorical (n, %)									
<0.70	82 (26.7)	28 (26.2)	20 (35.7)	9 (45.0)	2 (13.3)	2 (25.0)	7 (15.2)	14 (23.6)	.065
0.70-0.85	113 (36.8)	46 (43.0)	24 (42.9)	7 (35.0)	6 (40.0)	4 (50.0)	10 (21.7)	16 (29.1)	
>0.85	112 (36.5)	33 (30.8)	12 (21.4)	4 (20.0)	7 (46.7)	2 (25.0)	29 (63.0)	25 (45.5)	
Euroqol-VAS[3] (mean, 95% CI)	68.8 (66.7-70.9)	68.3 (64.6-72.0)	65.9 (62.0-70.0)	59.2 (50.0-68.4)	75.4 (64.4-86.4)	66.3 (57.4-75.1)	77.8 (73.3-82.3)	67.7 (61.9-73.4)	.003
Mobility (mean, 95% CI)[4]	1.54 (1.47-1.62)	1.55 (1.43-1.67)	1.71 (1,57-1,86)	1.65 (1.30-2.00)	1.33 (1.06-1.60)	1.75 (1.16-2.34)	1.28 (1.12-1.44)	1.56 (1.36-1.76)	.020
1 (n, %)	164 (53.4)	56 (52.3)	18 (32.1)	10 (50.0)	10 (66.7)	3 (37.5)	35 (76.1)	32 (58.2)	
2 (n, %)	119 (38.8)	43 (40.2)	36 (64.3)	7 (26.7)	5 (33.3)	4 (50.0)	9 (19.5)	15 (39.4)	
3 (n, %)	24 (7.8)	8 (7.4)	2 (3.6)	3 (6.7)	0 (0)	1 (12.5)	2 (4.3)	8 (14.5)	
Selfcare (mean, 95% CI)[4]	1.18 (1.13-1.22)	1.19 (1.10-1.27)	1.29 (1.16-1.41)	1.15 (0.98-1.32)	1.07 (0.92-1.21)	1.13 (0.83-1.42)	1.02 (0.98-1.07)	1.22 (1.07-1.36)	.077
1 (n, %)	259 (84.4)	90 (84.1)	40 (71.4)	17 (85.0)	14 (93.3)	7 (87.5)	45 (97.8)	46 (83.6)	
2 (n, %)	42 (13.7)	14 (13.0)	12 (28.6)	3 (15.0)	1 (6.7)	1 (12.5)	1 (2.2)	6 (10.9)	
3 (n, %)	6 (2.0)	3 (2.8)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	3 (5.5)	
Usual activities (mean, 95% CI)[4]	1.67 (1.60-1.75)	1.73 (1.61-1.85)	1.77 (1.63-1.90)	2.00 (1.66-2.34)	1.53 (1.18-1.89)	1.88 (1.34-2.41)	1.41 (1.22-1.61)	1.58 (1.38-1.78)	.010
1 (n, %)	132 (43.0)	40 (47.4)	15 (26.8)	5 (25.0)	8 (53.3)	2 (25.0)	31 (67.4)	31 (56.4)	
2 (n, %)	143 (46.6)	56 (52.4)	94 (69.6)	10 (5.0)	2 (40.0)	5 (62.5)	11 (23.9)	22 (29.1) 13	
3 (n, %)	32 (10.4)	11 (10.3)	2 (3.6)	5 (25.0)	1 (6.7)	1 (12.5)	4 (8.7)	(14.6)	
Pain and discomfort (mean, 95% CI)[4]	1.82 (1.76-1.88)	1.84 (1.74-1.94)	1.96 (1.84-2.09)	1.75 (1.54-1.96)	1.80 (1.49-2.11)	1.75 (1.36-2.14)	1.57 (1.40-1.73)	1.89 (1.71-2.08)	.089
1 (n, %)	80 (26.1)	25 (23.4)	7 (12.5)	5 (25.0)	4 (26.7)	2 (25.0)	21 (45.7)	16 (29.1)	
2 (n, %)	202 (65.8)	74 (69.2)	44 (78.6)	14 (75.0)	10 (66.7)	6 (75.0)	24 (52.2)	29 (52.8)	
3 (n, %)	25 (22.7)	8 (7.5)	5 (8.9)	0 (0)	1 (6.7)	0 (0)	1 (2.2)	10 (18.2)	
Anxiety and depression (mean, 95% CI)[4]	1.40 (1.34-1.46)	1.39 (1.29-1.49)	1.54 (1.37-1.70)	1.55 (1.27-1.83)	1.33 (1.06-1.60)	1.25 (0.86-1.64)	1.22 (1.09-1.34)	1.40 (1.25-1.55)	.020
1 (n, %)	194 (63.2)	67 (63.6)	30 (35.6)	10 (50.0)	10 (66.7)	6 (75.0)	36 (78.4)	35 (63.4)	
2 (n, %)	104 (33.8)	38 (35.5)	22 (39.3)	9 (45.0)	5 (33.3)	2 (25.0)	10 (21.6)	18 (32.7)	
3 (n, %)	9 (2.9)	2 (1.9)	4 (6.2)	1 (5.0)	0 (0)	0 (0)	0 (0)	2 (3.6)	

AI, autoinflammatory conditions; APS, antiphospholipid syndrome; CI, acronyms; CTDs, connective tissue diseases; IA, inflammatory arthritis; SD, standard deviation; VAS, visual analogue.

1. ANOVA for continuous and Chi-squared for categorical variables.
2. EuroQol utility score, calculated from the validated EQ-5D-5 L questionnaire. The five dimensions (mobility, self-care, usual activity, pain and discomfort, and anxiety and depression) were rated at five levels: 1 = no problem, 2 = slight problem, 3 = some problem, 4 = moderate problem, 5 = extreme problem. These ratings were used to calculate an overall utility score (range 0 (worst) to 1 (best)).
3. EuroQol-visual analogue scale (VAS) for the current overall health status, ranging from 0 (worst) to 100 (best).
4. The original five rating levels for each EuroQol dimension were pooled into three levels as follows: 1 = no problem, 2 = slight to some problem, 3 = moderate to extreme problem.

Table 3
Bivariable and multivariable analyses of factors associated with HR-QoL, using multinominal logistic regression.[1]

Variable	Bivariable (ref >0.85)	RRR (95% CI)	p-value	Multivariable (ref >0.85)	RRR (95% CI)	p-value[2]
Age per year increase (N=307)	<0.70 0.70-0.85	1.28 (0.86-1.93) 1.21 (0.83-1.74)	0.224 0.323			
Female sex (N=307)	<0.70 0.70-0.85	1.83 (1.00-3.35) 2.06 (1.17-3.62)	**0.036** **0.011**	<0.70 0.70-0.85	2.823 (1.18-6.76) 2.599 (1.03-6.57)	**0.020** **0.044**
Department (ref: ophthalmology) (N=307) Rheumatology Dermatology	<0.70 0.70-0.85 <0.70 0.70-0.85	6.97 (2.30-21.07) 4.01 (1.81-8.86) 4.11 (1.19-14.24) 1.29 (0.47-3.59)	**0.001** **0.001** **0.026** 0.624	<0.70 0.70-0.85 <0.70 0.70-0.85	9.54 (1.55-58.77) 9.26 (1.61-53.11) 12.50 (1.17-133.32) 7.75 (0.76-78-92)	**0.015** **0.013** **0.037** **0.084**
Disease duration per month (N=307)	<0.70 0.70-0.85	0.99 (0.98-1.00) 1.00 (0.99-1.01)	**0.044** 0.652	<0.70 0.70-0.85	1.00 (0.98-1.00) 1.00 (0.99-1.01)	0.115 0.575
BMI per index point increase (N=222)	<0.70 0.70-0.85	1.02 (0.96-1.08) 0.99 (0.93-1.05)	0.480 0.725			
ESR per mm/hour increase (N=281)	<0.70 0.70-0.85	1.04 (1.01-1.06) 1.02 (0.99-1.04)	**0.006** 0.226	<0.70 0.70-0.85	1.01 (0.99-1.04) 0.98 (0.94-1.01)	0.358 0.146
CRP per mg/L increase (N=283)	<0.70 0.70-0.85	1.03 (1.00-1.07) 1.03 (1.00-1.07)	0.077 0.068	<0.70 0.70-0.85	1.01 (0.97-1.00) 1.05 (1.00-1.01)	0.601 0.061
Smoking (ref: never smoked) (N=279) Past smoker Smoker	<0.70 0.70-0.85 <0.70 0.70-0.85	2.46 (1.24-4.90) 1.26 (0.69-2.28) 3.79 (1.45-9.90) 2.46 (1.04-5.81)	**0.010** 0.453 **0.007** **0.041**	<0.70 0.70-0.85 <0.70 0.70-0.85	4.20 (1.67-10.59) 1.93 (0.85-4.37) 3.38 (1.03-11.09) 3.22 (1.13-9.24)	**0.002** 0.114 **0.045** **0.029**
Alcohol use (ref: never used) (N=275) Past alcohol user Current alcohol user	<0.70 0.70-0.85 <0.70 0.70-0.85	1.99 (0.70-5.66) 1.41 (0.52-3.80) 0.64 (0.30-1.37) 0.59 (0.30-1.17)	0.198 0.500 0.248 0.133			
Therapy (ref: no current treatment) (N=307) – NSAIDs and/or steroids – Monotherapy cDMARDs (with/without combination, bDMARD use excluded) – bDMARDs (with/without combination)	<0.70 0.70-0.85 <0.70 0.70-0.85 <0.70 0.70-0.85	1.52 (0.65-3.58) 0.66 (0.29-1.51) 1.26 (0.59-2.67) 1.25 (0.66-2.36) 3.07 (1.29-7.29) 1.15 (0.49-2.68)	0.337 0.327 0.551 0.489 **0.011** 0.752	<0.70 0.70-0.85 <0.70 0.70-0.85 <0.70 0.70-0.85	4.77 (0.89-25.62) 1.02 (0.24-4.34) 1.48 (0.36-6.05) 0.71 (0.24-2.08) 5.28 (1.12-25.04) 0.528 (0.14-2.07)	0.069 0.978 0.586 0.243 **0.036** 0.359
mCCI per index point increase (N=307)	<0.70 0.70-0.85	1.13 (0.92-1.39) 1.16 (0.96-1.41)	0.235 0.122			

BMI, body mass index; bDMARDs, biological disease modifying antirheumatic drugs, cDMARDs, conventional disease modifying antirheumatic drugs; CRP, CTDs, connective tissue diseases; ESR, estimated sedimentation rate; iv, intravenous; mCCI, modified Charlson Comorbidity Index, NSAIDs, non-steroidal anti-inflammatory drugs; RRR, relative risk ratio.
1. Variables that had a *p*-value of <0.10 in the bivariable logistic multinominal logistic regression analysis were included in the multivariable analysis.
2. *P*-values <.05 are shown in bold.

3.5. HR-QoL determinants

Variables that were associated with a low EQ-5D-5 L utility score (<0.70) in bivariable multinomial models were female sex, rheumatological IMIDs or psoriasis (compared to uveitis), shorter disease duration, higher ESR, smoking or having smoked in the past, and currently using bDMARDs. In the multivariable multinomial model, all these variables with the exceptions of disease duration and ESR remained significant. Subgroup analysis of risk factors in the IMID categories was not possible because of small numbers in each category. (See Table 4.)

4. Discussion

Our study assessed and compared HR-QoL in patients with IMIDs in a unique multidisciplinary cohort. Patients with IMIDs had a lower mean HR-QoL EQ-5D-5 L utility score (0.75) compared to the general Dutch population (0.89) [15]. Furthermore, we found differences in HR-QoL across IMIDs: patients with inflammatory arthritis, vasculitis and psoriasis had the lowest mean score and patients with uveitis the highest. A low utility score (<0.70) was significantly associated with female sex, rheumatological IMID or psoriasis (compared to uveitis), current or past smoking, and current use of bDMARDs in a multivariable model. Also, in the analysis of the separate domains of the EQ-5D-5 L, there were significant differences between IMIDs, with regard to mobility, usual activities, selfcare and anxiety and depression. Variation in HR-QoL between IMIDs was observed in other cohorts from Rheumatology departments in Western societies as well. A Canadian cohort investigated HR-QoL in rare CTDs using the SF-36 [16]. Patients with myositis (N = 25) had lower scores in the physical and mental domains compared to patients with SLE (N = 118), systemic sclerosis (N = 108) and RA (N = 64). In another Canadian study comparing subjects with systemic sclerosis (N = 34), SLE (N = 74) and RA (N = 42), scores were lowest in SSc and best in SLE [17]. In a Norwegian study, HR-QoL was assessed in patients with RA (N = 3898) and psoriatic arthritis (N = 1515), using the SF-36 [7]. In both groups, HR-QoL was decreased compared to the general Norwegian population and similar between the patient groups. After six months of DMARD treatment, HR-QoL scores improved in both groups, although the gain was larger in RA patients.

The differences observed within IMIDs in our study could reflect the disease-specific symptoms and related impairments. The high HR-QoL index scores in the uveitis patients in our study, may be because of the

Table 4
Bivariable analyses of factors associated with HR-QoL, using multinominal logistic regression[1] in CTDs, IA, uveitis and psoriasis.

Variable	Bivariable (ref >0.85)	CTDs RRR (95% CI)	p-value[2]	IA RRR (95% CI)	p-value[2]	Uveitis RRR (95% CI)	p-value[2]	Psoriasis RRR (95% CI)	p-value[2]
		N=104		**N=56**		**N=46**		**N=55**	
Age per year increase	<0.70	1.04 (1.00-1.08)	0.073	0.98 (0.95-1.03)	0.434	1.01 (0.97-1.06)	0.212	0.99 (-.95-1.03)	0.652
	0.70-0.85	1.02 (0.99-1.06)	0.224	1.00 (0.96-1.04)	0.994	1.03 (0.98-1.08)	0.573	1.02 (0.97-1.06)	0.478
		N=104		**N=56**		**N=46**		**N=55**	
Female sex	<0.70	4.50(0.87-23.30)	0.073	1.47 (0.35-6.17)	0.599	1.25 (0.24-6.29)	0.211	1.94 (0.45-7.64)	0.341
	0.70-0.85	3.50(0.95-12.85)	0.059	2.57(0.62-10.74)	0.159	3.00(0.54-16.77)	0.787	0.96 (0.24-3.90)	0.956
		N=104		**N=54**		**N=46**		**N=46**	
Disease duration per month	<0.70	0.98 (0.96-1.00)	**0.021**	0.98 (0.96-1.00)	0.061	1.01 (0.98-1.05)	0.501	1.00 (0.98-1.03)	0.715
	0.70-0.85	1.00 (0.99-1.01)	0.896	0.98 (0.96-1.00)	**0.030**	1.02 (0.98-1.05)	0.319	1.01 (0.99-1.03)	0.427
		N=66		**N=41**		**N=35**		**N=52**	
BMI per index point increase	<0.70	1.11 (0.95-1.29)	0.200	0.93 (0.81-1.07)	0.321	1.08 (0.91-1.29)	0.392	1.03 (0.92-1.16)	0.576
	0.70-0.85	0.99 (0.84-1.16)	0.910	0.99 (0.87-1.12)	0.874	1.03 (0.86-1.23)	0.725	1.01 (0.90-1.14)	0.855
		N=105		**N=41**		**N=30**		**N=51**	
ESR per mm/hour increase	<0.70	1.03 (0.99-1.07)	0.121	1.05 (0.97-1.14)	0.224	1.10 (0.98-1.22)	0.097	1.09 (0.98-1.20)	0.107
	0.70-0.85	1.00 (0.96-1.04)	0.927	1.03 (0.95-1.12	0.470	0.99 (0.85-1.16)	0.927	1.05 (0.94-1.16)	0.407
		N=105		**N=54**		**N=43**		**N=50**	
CRP per mg/L increase	<0.70	0.96 (0.89-1.04)	0.339	1.13 (0.96-1.33)	0.146	1.03 (0.87-1.23)	0.695	1.05 (0.94-1.17)	0.360
	0.70-0.85	0.98 (0.92-1.04)	0.489	1.14 (0.96-1.34)	0.133	1.01 (0.84-1.21)	0.939	1.05 (0.94-1.17)	0.382
		N=104		**N=55**		**N=45**		**N=32**	
Smoking (ref:never smoked)									
Past smoker	<0.70	5.71(1.71-19.14)	**0.005**	NA		NA		0.25 (0.03-2.24)	0.215
	0.70-0.85	2.65 (0.92-7.60)	0.070					0.42 (0.05-3.31)	0.407
Smoker	<0.70	4.29(0.93-19.80)	0.062					0.50 (0.37-6.68)	0.600
	0.70-0.85	2.35 (0.60-9.20)	0.219					1.00 (0.91-11.03)	1.000
		N=102		**N=53**		**N=45**		**N=32**	
Alcohol use (ref:never used)									
Past alcohol user	<0.70	0.62 (0.16-2.36)	0.479	0.10(0.65-154.4)	0.099	1.33(0.09-20.71)	0.837		
	0.70-0.85	1.30 (0.23-7.38)	0.770	2.00 (0.15-26.7)	0.600	0.89(0.06-12.25)	0.930	NA	
Current alcohol user	<0.70	1.39 (0.22-8.92)	0.729	2.75(0.40-18.88)	0.303	0.94 (0.14-6.23)	0.950		
	0.70-0.85	0.65 (0.19-2.22)	0.495	1.08 (0.23-5.06)	0.919	0.94 (0.19-4.76)	0.942		
		N=104		**N=55**		**N=46**		**N=55**	
Therapy (ref: no current treatment)		NA		NA		NA			
– NSAIDs and/or steroids	<0.70							1.50 (0.18-12.78)	0.711
	0.70-0.85							0.50 (0.04-6.02)	0.585
– Monotherapy cDMARDs (with/without combination bDMARD use excluded)	<0.70							4.50 (0.57-35.52)	0.154
	0.70-0.85							1.50 (0.16-13.75)	0.720
– bDMARDs (with/without combination)	<0.70							1.93 (0.39-9.60)	0.423
	0.70-0.85							1.93 (0.46-8.05)	0.368
		N=104		**N=55**		**N=46**		**N=55**	
mCCI per index point increase	<0.70	1.33 (0.87-2.02)	0.187	1.16 (0.71-1.90)	0.551	1.09 (0.65-1.84)	0.740	0.76 (0.43-1.33)	0.337
	0.70-0.85	1.30 (0.88-1.91)	0.190	1.13 (0.70-1.83)	0.606	1.31 (0.83-2.08)	0.245	1.25 (0.79-1.97)	0.338

BMI, body mass index; bDMARDs, biological disease modifying antirheumatic drugs, cDMARDs, conventional disease modifying antirheumatic drugs; CRP, C-reactive protein; CTDs, connective tissue diseases; ESR, estimated sedimentation rate; IA, inflammatory arthritis; iv, intravenous; mCCI, modified Charlson Comorbidity Index, NSAIDs, non-steroidal anti-inflammatory drugs; RRR, relative risk ratio.

1. Variables that had a p-value of <0.05 in the bivariable logistic multinominal logistic regression analysis were included in the multivariable analysis.
2. P-values $<.05$ are shown in bold.
3. NA is Not Analysable due to small n.

lack of systemic symptoms that impair mobility and produce pain. They might also be explained by a relatively mild disease activity, illustrated by a low consumption of anti-inflammatory medication.

We found that current bDMARD users had a lower HR-QoL compared to patients who did not use bDMARDs. This could be due to reverse causality: these patients likely had higher disease activity that triggered treatment by bDMARDs. Longitudinal data are needed to determine if bDMARD use eventually improves HR-QoL. In longitudinal studies by others, a good clinical response to bDMARDs was correlated with better HR-QoL in RA, psoriatic arthritis, and psoriasis patients [18,19]. Current and past smoking was associated with poorer HR-QoL scores. This is in line with several earlier reports that also showed a negative association of smoking and HR-QoL both in the general population and in patients with chronic IMIDs [20–24]. In addition, in many inflammatory conditions, tobacco use has been shown to be associated with disease activity and organ damage [25,26].

Our study had some limitations. We were not able to recruit all new patients with relevant IMIDs during the enrollment period and we did not take a random sample of them either. Our sample is, therefore, a convenience sample. This means that the results may not be generalizable to other patient populations. In addition, the data reported here are cross-sectional and can therefore not assess changes over time. We did not collect data on disease-specific disease activity scores. It would have been of interest to correlate such activity scores to the CRP and ESR measurements and the HR-QoL utility scores. However, because our study included patients with several different IMIDs, direct comparisons between such scores would have been difficult, and for some IMIDs, no consensus disease activity scoring system exists. Finally, we used the EQ-5D-5 L questionnaire, while earlier studies often used the SF-36 questionnaire. Direct comparisons between our study and these older studies are therefore not possible. However, we prefer the EQ-5D-5 L over the SF-36 because it is more concise and easier to complete.

The strength of this study is that we enrolled a large number of patients with different IMIDs from different departments in our hospital using standardized assessment of HR-QoL and several other important variables. To our knowledge, this is the first multidisciplinary IMID cohort in which HR-QoL was assessed in such a large group of patients.

5. Concluding remarks

In conclusion, we identified differences in HR-QoL across IMIDs in a large, multidisciplinary cohort in the Netherlands. Several factors were associated with a decreased HR-QoL. The results from our study indicate that HR-QoL and the contributing factors deserve attention in care in patients with IMIDs. Long-term follow up is warranted to monitor HR-QoL over time and assess the impact of interventions on HR-QoL.

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