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OBSERVATIONAL RESEARCH

The impact of obesity and overweight on rheumatoid arthritis patients: real-world insights from a biologic and targeted synthetic DMARDs registry

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Abstract

The Impact of Obesity and Overweight on Rheumatoid Arthritis Patients: Real-World Insights from a Biologic and Targeted Synthetic DMARDs Registry. The management of rheumatoid arthritis (RA) has advanced with biological and targeted synthetic disease-modifying anti-rheumatic drugs (b/tsDMARDs). However, obesity, a common comorbidity, impacts treatment and disease progression efficacy. This article examines the association between body weight, activity of the disease and the effectiveness of b/tsDMARDs in RA patients. This multicenter observational cohort study, conducted as part of the BioSTAR Registry, involved a total of 856 patients diagnosed with RA (168 males and 688 females). Patients were separated into groups based on BMI: Group 1 ("normal BMI: ≥18.5 to <25 kg/m^2 or underweight BMI: <18.5 kg/m^2") and Group 2 ("overweight BMI: ≥25 to <30 kg/m^2 or obese BMI: ≥30 kg/m^2"). Baseline socio-demographic and clinical data, medication use, switching status, and total glucocorticoid dose (mg-year) were collected. Age, disease duration, disease activity scores were considerably higher in obesity/overweight patients. Remission rates were lower in obese/overweight patients (35.6% and 25.9% in group 1 and 2 respectively; $p=0.026$). The cumulative steroid doses, number of biologics and switches were similar between groups, regardless of pharmacological mechanisms. Regression analysis indicated that BMI was one of the factors affecting DAS28-CRP. The obesity/overweight rate is as high as 70.4% in RA patients. While obesity/overweight is related to enhanced disease activity, lower remission rates in RA, its effect on the choice and switch rates of b/tsDMARDs appears minimal. Clinical effectiveness remains consistent across drug classes, regardless of BMI.

Keywords Biological therapy · Comorbidity · Obesity · Rheumatoid arthritis

Introduction

Rheumatoid arthritis (RA) is a systemic autoimmune disorder characterized by persistent joint inflammation and gradual synovial tissue destruction, affecting approximately 0.5–1% of the global population. The pathogenesis of RA is multifactorial, encompassing genetic susceptibility, immune dysregulation, and environmental triggers [1].

Among the environmental contributors, obesity has gained attention as a notable risk factor for RA onset [2]. Nonetheless, studies investigating this relationship have produced inconsistent findings [3–6]. Studies have shown that individuals with a higher body mass index (BMI) are more likely to develop rheumatoid arthritis (RA), particularly its seronegative variants [3, 4]. A systematic review reported that obesity increases the risk of developing RA by approximately 3.45 times [4]. Additionally, about two-thirds of RA patients are either overweight or obese, reflecting the prevalence seen in the general population [5]. Contrarily, a recent Korean study found that obesity was associated with

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a reduced risk of RA, especially among women and those maintaining a normal waist circumference [6].

Although obesity's precise role in the development of RA remains incompletely understood, several biological pathways provide insight into its contributory role. Adipose tissue secrets various adipokines, such as leptin and resistin, which can exacerbate joint inflammation and contribute to the systemic inflammatory state observed in RA patients [7, 8].

Adipose tissue secretes pro-inflammatory cytokines, including IL-6 and TNF-α, which play a critical role in the development of rheumatoid arthritis. These cytokines exacerbate synovial inflammation and can diminish the therapeutic effectiveness of [7, 8].

Furthermore, obesity alters immune function, potentially leading to an exaggerated immune response in RA patients. This dysregulation can result in increased disease activity and progression over time [4]. The convergence of these inflammatory processes complicates clinical management and may contribute to diminished responsiveness to treatment.

Achieving remission is a primary goal in RA treatment, with options including targeted synthetic DMARDs (tsDMARDs), conventional synthetic disease-modifying antirheumatic drugs (csDMARDs), and biologic DMARDs (bDMARDs) [9]. However, responses to treatment can vary widely among patients, and not everyone archives clinical remission and low disease activity [10]. Research has associated obesity with poorer clinical outcomes in rheumatoid arthritis, demonstrating that patients with higher BMI are significantly less likely to reach and maintain disease remission than those with normal weight [11, 12].

The connection between obesity or increased BMI and response to treatment varies across studies, and nearly all of these studies have been conducted in RA patients receiving biological therapy [10, 13]. To the best of our knowledge, the literature is scarce in examining the impact of obesity or being overweight on patients with RA who are treated with tsDMARDs. The aim of our study is to examine the effects of obesity across a broader spectrum of therapies, including TNF inhibitors, other biologics, and tsDMARDs. In this regard the relationship between obesity/overweight and disease activity, treatment response, and drug switch rates in RA patients receiving both tsDMARDs and bDMARDs was assessed.

Methods

This multi-center observational cohort study involved 856 cases from the BioSTAR ("Biological and Targeted Synthetic Disease-Modifying Antirheumatic Drugs Registry") from February 1, 2019, to July 31, 2024. The BioSTAR registry collects routinely collected data from patient-reported outcomes involving lifestyle habits, demographics, details regarding antirheumatic medication, and clinical endpoints, and rheumatology visits.

For this study, patient medical information was evaluated as of July 2024. Approval for this research was granted by the institutional ethics review board (Ethical committee number: E1-23-4387). All procedures adhered to the ethical standards set forth in the Declaration of Helsinki (1964) and its subsequent amendments. Prior to participation, every subject provided written informed consent.

Study population

This study involved adult individuals (> 18 years) with RA, diagnosed according to the 2010 ACR ("American College of Rheumatology")/EULAR ("European League Against Rheumatism") classification criteria [14], who were registered in BıoSTAR and initiated treatment with TNF-α blockers, abatacept, tocilizumab, rituximab, or Janus kinase inhibitors as b/tsDMARDs between 1 February 2019 and 31 July 2024.

Participants were categorized by BMI into four groups: obese (BMI ≥ 30 kg/m^2), overweight (BMI 25–29.9 kg/m^2), normal weight (BMI 18.5–24.9 kg/m^2), and underweight (BMI < 18.5 kg/m^2) [15]. Group 1 included normal-weight and underweight individuals, while Group 2 included obese and overweight participants.

Baseline socio-demographic and clinical characteristics were extracted from relevant databases for analysis. The study examined several potential covariates, including: sex, age, C-reactive protein (CRP; mg/L), disease duration, Disease Activity Score of 28 joints (DAS28) and its components ["(erythrocyte sedimentation rate (ESR; mm/h) and CRP (mg/L)"], patient global assessment (NRS 0–10), swollen joint count (SJC), and tender joint count (TJC). The Simplified Disease Activity Index (SDAI) and Clinical Disease Activity Index (CDAI) and were used to assess disease activity. DAS28-CRP and DAS28-ESR scores more than 5.1, CDAI scores over 22, or SDAI scores over 26 were considered indicative of high disease activity [16].

Patient-reported outcome measures were documented, encompassing VAS (Visual Analog Scale) scores for both physician global assessments and patient, along with pain and fatigue evaluations. Additionally, patients were evaluated according to the 2016 ACR fibromyalgia criteria, including the Symptom Severity Scale (SSS) and Widespread Pain Index (WPI) scores [17]. The RA Impact of Disease (RAID) and Health Assessment Questionnaire (HAQ) scores were obtained [18, 19].

Status of alcohol use and smoking ("current, former, or never"), cigarette consumption (expressed in packs per year), level of education, and comorbidities were also recorded.

The current use of b/tsDMARDs, treatment switching status, and the number of switches were documented from patients' medical files. Medications were grouped by their pharmacological action mechanisms for the analysis, including rituximab, tocilizumab, TNF-α blockers (adalimumab, etanercept, golimumab, infliximab, sertolizumab-pegol), abatacept, and Janus kinase inhibitors (baricitinib, tofacitinib, upatacitinib). Glucocorticoid use was assessed based on the prednisolone equivalent dose in all patients. The total number of years of steroid use and the daily dose in milligrams were recorded. Cumulative steroid dose was calculated by multiplying the daily prednisolone equivalent dose by the number of years of use and was recorded in mg-years.

Statistical analysis

G* power 3.1.9.4 program was utilized for the calculation of the post-hoc power of the study. The effect size was 0.24. The power of the study was 0.89 ["α (Type I error) was 0.05 and β (Type II error) was 0.20"].

Statistical analyses were done using the SPSS ("Statistical Package for Social Sciences") for Windows 23 software. To assess normality, the Shapiro-Wilk test was employed. Descriptive statistics, including median (minimum-maximum), mean (standard deviation), counts, and percentages, were calculated. For comparisons between two groups, the Mann-Whitney U test was utilized. The Kruskal-Wallis H test was employed to compare the median values (or mean ranks) of more than two groups. The homogeneity of categorical variable distributions was assessed using the Fisher's exact test or chi-square test. The Spearman rank correlation coefficient was used, with values ranging from −1 to +1. Binary logistic regression analysis was performed to assess the factors related to disease activity. Variable selection was performed using univariate analyses and at least moderately significant variables were included. The statistical significance for P-value was considered to be $P<0.05$.

Results

A total of 856 cases with RA were involved, with a median age of 57 years and a median BMI of 26.0. Obesity or overweight was observed in 603 (34.2% obese, and 36.2% overweight) patients. The overweight/obese group exhibited a significantly increased mean age (58.0 years) in comparison to the underweight/normal group (52.0 years), with this age difference being statistically significant ($p<0.001$). Females constituted the majority across all categories (80.3% overall) but were particularly over-represented in the overweight/obese group (83.9%) in comparison to the underweight/normal group (71.9%), with this difference also being statistically significant ($p<0.001$).

Educational level was statistically different between the groups: 65.2% of overweight/obese individuals had only primary education, compared to 43.1% in underweight/normal patients. Only 7% of overweight/obese participants had attained a college/university education, compared to 20.9% in the underweight/normal group.

Tobacco use patterns showed distinct variations: the current smoking prevalence was nearly twice as high in the underweight/normal group. However, no significant difference was observed in pack-year exposure between the groups (median 20 vs. 15, $p=0.545$). The prevalence of hypertension and diabetes increased with BMI, and the comorbidity burden was substantially greater in those with higher BMI. Baseline characteristics are presented in Table 1.

Overweight/obese RA cases exhibited significantly increased CRP levels and greater disease activity in comparison to their underweight/normal-weight counterparts, as evidenced by elevated DAS28-CRP (3.53 vs. 3.20; $p=0.019$) and SDAI scores (14.79 vs. 12.40; $p=0.011$). The remission rates differed significantly between groups: 35.6% (90 patients) in the underweight/normal weight group versus 25.9% (156 patients) in the overweight/obese group. Overweight/obese patients experienced a higher disease duration ($p=0.004$).

There was no significant difference between the groups in regards to pain, fatigue, WPI, SSS, swollen and tender joint scores, HAQ scores, cumulative steroid dose and switch number and percentage of b/tsDMARDs. Clinical and laboratory parameters, switching profiles between the groups are provided in Table 2.

Patients were also evaluated in four separate groups based on body mass index. Age, female gender ratio, disease duration, comorbidity rate, and disease activity were higher in the obese group, while switch rates and cumulative steroid doses were similar (Supplementary Material).

Table 3 presents the distribution of b/tsDMARDs across different BMI categories, including the percentage and number of cases in each of the categories for each medication. The number and rates of drug use were similar between the groups.

Patients were categorized into drug subgroups based on similar pharmacological properties according to the DMARDs they were using. It was observed that DAS28-CRP, remission rates and BMI values were similar across the different DMARDs groups. The data is presented in Table 4.

Table 1 Patient demographics and comorbid conditions

	Total $N=856$	Underweight/normal $N=253$	Overweight/obese $N=603$	p
Age (years)	Median (57.0) Min; max (20;89)	Median (52) Min; max (20;89)	Median (58.0) min; max (20;85)	**<0.001**
Gender *n* (%)				
Female	688 (80.4)	182 (71.9)	506 (83.9)	**<0.001**
Male	168 (19.6)	71 (28.1)	97 (16.1)	
Educational status *n* (%)				
Primary school	502 (58.6)	109 (43.1)	393 (65.2)	**<0.001**
High school	259 (30.3)	91 (36.0)	168 (27.9)	
College/university	95 (11.1)	53 (20.9)	42 (7.0)	
Smoking status, *n* (%)				
Never smoked	604 (70.6)	160 (63.2)	444 (73.6)	**0.001**
Ex smoker	117 (13.7)	39 (15.4)	78 (12.9)	
Already smoking	117 (13.7)	51 (20.2)	66 (10.9)	
Not knowned	18 (2.1)	3 (1.2)	15 (2.5)	
Smoking (pack/year)	17 (1–80)	20 (1–50)	15 (1–80)	0.545
Alchol consumption, *n* (%)				
Never consumed	787 (92.0)	222 (87.7)	565 (93.9)	0.008
Ex consumer	11 (1.3)	4 (1.6)	7 (1.2)	
Already consuming	27 (3.2)	16 (6.3)	11 (1.8)	
Not knowned	30 (3.5)	11 (4.3)	19 (3.2)	
Comorbidity, *n* (%)	360 (42.5)	74 (29.6)	286 (47.8)	**0.001**
Hypertension, *n* (%)	240 (27.9)	34 (13.4)	206 (34)	**<0.001**
Diabetes Mellitus, *n* (%)	113 (13.1)	17 (6.7)	96 (15.9)	**<0.001**

Table 3 Distribution of b/tsdmards by body mass index categories

b/tsDMARDs	Underweight/normal *n* (%)	Overweight/obese *n* (%)	Total *n* (%)	p
Adalimumab	46 (18.2)	113 (18.7)	159 (18.6)	0.442
Certolizumab pegol	13 (5.1)	35 (5.8)	48 (5.6)	
Etanercept	48 (19.0)	83 (13.8)	131 (15.3)	
Golimumab	19 (7.5)	50 (8.3)	69 (8.1)	
Infliximab	6 (2.4)	25 (4.1)	31 (3.6)	
Rituximab	48 (19.0)	107 (17.7)	155 (18.1)	
Abatacept	12 (4.7)	22 (3.6)	34 (4.0)	
Tocilizumab	36 (14.2)	77 (12.8)	113 (13.2)	
Baricitinib	1 (0.4)	4 (0.7)	5 (0.6)	
Tofacitinib	22 (8.7)	83 (13.8)	105 (12.3)	
Upatacitinib	2 (0.8)	4 (0.7)	6 (0.7)	
Total	253	603	856	

b/tsDMARDs Biologic/targeted synthetic disease modifying anti rheumatic drugs

Table 2 Clinical and laboratory parameters, switching profiles between the groups

	Underweight/normal Median (min–max)	Overweight/obese Median (min–max)	p
Disease duration (year)	11 (1–34)	12 (1–50)	**0.004**
Age of RA onset	38 (20–75)	44 (20–72)	**<0.001**
VAS doctor global	40.00 (0–95)	40.00 (0–100)	0.647
VAS patient global	50.00 (0–100)	50.00 (0–100)	0.391
VAS pain	40.00 (0–100)	40.00 (0–100)	0.092
VAS fatigue	50.00 (0–100)	50.00 (0–100)	0.703
Low density lipoprotein (mg/dL)	110.50 (40–295)	123.00 (30–295)	0.007
High density lipoprotein (mg/dL)	52.00 (20–107)	53.00 (20–107)	0.856
Triglyiceride (mg/dL)	112.00 (40–555)	131 (47–555)	**0.005**
Cholesterole (mg/dL)	190 (95–380)	200 (95–380)	**0.006**
25(OH)D3 Vitamin(ug/L)	20.96 (2.06–140)	19.63 (2.3–150)	0.431
C-reactive protein (mg/L)	1.20 (0–91.20)	2.30 (0–214)	**<0.001**
Erytrocyte sedimantation rate (mm/h)	21.00 (1–118)	23.00 (1–120)	0.338
DAS28-CRP	3.20 (1.22–7.92)	3.52 (0.96–8.75)	**0.019**
DAS28-CRP, *n* (%)			
Remission	90 (35.6)	156 (25.9)	**0.026**
Low disease activity	56 (22.1)	155 (25.7)	0.140
Moderate disease activity	85 (33.6)	217 (36.0)	
High disease activity	22 (8.7)	75 (12.4)	
Tender joint score	3 (0–28)	4 (0–28)	
Swollen joint score	1 (0–20)	2 (0–25)	0.742
CDAI	10.00 (0–63)	11.00 (0–64)	0.382
SDAI	12.40 (0.30–76)	14.79 (0–76)	**0.011**
HAQ	0.50 (0–3.00)	0.60 (0–2.85)	0.056
RAID	3.54 (0–9.85)	3.97 (0–10.00)	0.091
Widespread Pain Index	3.00 (0–19.00)	3.00 (0–19.00)	0.332
Symptom Severity Score	3.00 (0–10)	4.00 (0–12.00)	0.255
Fibromyalgia Severity Scale	5.00 (0–28.00)	6.00 (0–28.00)	0.091
B/tsDMARD switch number, *n* (%)			
No switch	168 (66.4)	407 (67.5)	0.269
1 switch	60 (23.7)	119 (19.7)	
2 or more switch	25 (9.9)	77 (12.8)	
Cumulative steroid dose (mg/year)	10.00 (2.50–1095)	5.00 (0.50–500)	0.150

BMI Body Mass Index, *VAS* Visual Analog Scale, *CDAI* The Clinical Disease Activity Index, *SDAI* Simplefied Disease Activity Index, *HAQ* Health Assessment Questionnaire, *RA* Rheumatoid arthritis, *RAID* Rheumatoid Arthritis Impact of Disease, *b/tsDMARDs* Biologic/targeted synthetic disease modifying anti rheumatic drugs

Correlation analysis demonstrated a positive relation between BMI and age, disease duration, CRP, SDAI,

Table 4 BMI and DAS28-CRP values between drug subgroups

Drug subgroups	BMI median (min-max)	*p*	DAS28-CRP median (min-max)	*p*	Remission rate *n* (%)	*p*
TNF α inhibitors	27.66 (16.22–44.44)	0.497	3.40 (0.96–8.50)	0.350	132 (30.1)	0.446
Rituximab	27.69 (17.26-40.00)		3.45 (1.44–7.14)		41 (26.5)	
Tocilizumab	27.99 (17.30-42.22)		3.15 (1.35–7.04)		36 (31.9)	
Abatacept	27.87 (20.20-39.11)		3.99 (2.11–8.75)		8 (23.5)	
Targeted synthetic DMARDs	28.75 (18.82–44.44)		3.50 (1.70–7.92)		29 (25.0)	

BMI Body Mass Index, *DAS28* Disease Activity Score of 28 Joints, *CRP* C-Reactive Protein, *DMARDs* Disease Modifying anti Rheumatic Drugs

Table 5 Correlation analysis between BMI and clinical and laboratory variables

	Body Mass Index	
	r	p
Age	0.244	**<0.001**
Disease duration	0.110	**0.001**
25 (OH)3 Vitamin D	− 0.078	0.494
Number of comorbidities	0.210	**<0.001**
C-reactive protein	0.171	**<0.001**
VAS pain	0.071	**0.042**
VAS patient global	0.039	0.266
DAS28 CRP	0.118	**0.002**
CDAI	0.047	0.227
SDAI	0.129	**0.001**
HAQ	0.069	**0.048**
RAID	0.065	0.063
Switch number	0.031	0.337
Cumulative steroid dose	− 0.084	**0.032**

BMI Body Mass Index, *VAS* Visual Analog Scale, *CDAI* The Clinical Disease Activity Index, *SDAI* Simplefied Disease Activity Index, *HAQ* Health Assessment Questionnaire, *RAID* Rheumatoid Arthritis Impact of Disease

DAS28-CRP, and HAQ scores. The details of these correlations are provided in Table 5.

Factors that correlates to disease activity were evaluated by logistic regression analysis. Body mass index, VAS pain, and comorbidity were discovered to be related with disease activity. The analysis results are summarized in Table 6.

Discussion

This study aimed to evaluate the occurrence of obesity/overweight among RA patients receiving b/tsDMARD therapy, exploring its connection with clinical variables and treatment outcomes. In this study, 856 patients with RA were analyzed, with a mean age of 54.96 years. A significant proportion (70.4%) of patients were overweight or obese, and this group exhibited higher mean age and a greater prevalence of female patients. Overweight/obese patients had heightened CRP levels and greater disease activity (SDAI and DAS28-CRP), lower remission rates compared to underweight/normal-weight individuals. However, no significant difference was found in pain, fatigue, or treatment across BMI categories. Positive relation was discovered between BMI and disease activity. Regression analysis showed that BMI was associated with disease activity. Upon examining the medications, switch rates and utilization for biologic and targeted synthetic DMARDs, the cumulative steroid dose revealed no significant differences across BMI categories.

The overweight and obesity rates observed in our study were consistent with those reported in the literature, though slightly higher than the rates found in three large German RA databases [20] and the National Data Bank for Rheumatic Diseases [21] which indicated that approximately two-thirds of RA patients are either overweight or obese. The results of our study align with broader epidemiological trends that underscore obesity as a common comorbidity in RA [4].

In this study, female-predominant gender distribution was observed in both groups; however, the percentage of women

Table 6 Binary logistic regression analysis showing the association between disease activity and related factors

Disease activity DAS28-CRP	B	SE	*p*	Exp(B)	95%CI	
Constant	0.574	0.198	0.004	1.775		
Age	−0.078	0.031	0.124	0.925	0.871	0.983
Gender	−1.106	0.654	0.091	0.331	0.092	1.192
Body Mass Index	0.184	0.064	**0.004**	1.202	0.998	1.014
VAS Pain	0.023	0.011	**0.043**	1.023	1.001	1.046
Comorbidity	0.791	0.326	**0.015**	2.206	1.164	4.181

B regression coefficient, *SE* Standard error, *Exp(B)* Odds ratio, *Cl* Confidence interval

in the obese/overweight group was discovered to be statistically significant at 83.8%. Two large-scale prospective studies, the Nurses' Health Study II (NHSII) and Nurses' Health Study (NHS), have demonstrated a significant association between excess body weight and a higher risk of developing rheumatoid arthritis (RA) in women. Findings suggest that both overweight and obesity contribute to a heightened susceptibility to RA in women, potentially due to systemic inflammation and metabolic dysregulation linked to adiposity [21].

Obese/overweight patients in our study also had a longer disease duration and a positive correlation was found between BMI and disease duration. A German study corroborated this, establishing a link between BMI and the age of disease onset [20]. A large prospective cohort study found that being overweight or obese at 18 years of age was associated with a 37% increased risk of developing RA [22].

Disease activity scores and CRP levels were significantly higher while remission rates were lower in obese and overweight groups. Additionally, regression analysis revealed that BMI was related with disease activity. These results are consistent with existing literature that emphasizes the link between obesity and an enhanced immune response in RA patients [20]. These findings further underscore and the pro-inflammatory role of adipose tissue, which secretes cytokines such as leptin and adiponectin that exacerbate systemic inflammation [4]. Recent studies consistently affirm that obesity adversely affects responses to biological treatments among RA patients; one particular study involving 793 participants indicated that untreated early RA individuals classified as obese exhibited diminished chances for achieving remission compared to those maintaining normal weight statuses—highlighting correlations between higher disease activity scores alongside reduced probabilities for reaching clinical remission at multiple follow-up intervals extending up to 48 weeks [23].

The literature presents conflicting findings regarding the impact of BMI on responses to various biologic treatments. Several studies suggest that obesity impairs the efficacy of TNF inhibitors, such as etanercept and infliximab. A study assessing etanercept, infliximab, and abatacept found no substantial differences in remission rates across BMI categories, although abatacept showed potential advantages for obese individuals due to its distinct mechanism of action compared to TNF inhibitors [24]. However, a Swiss registry study did not observe any direct benefit from abatacept over adalimumab across BMI categories [25].

In contrast, the impact of obesity on the efficacy of tocilizumab appears to differ markedly from that observed by TNF inhibitors. Emerging evidence suggests that although obesity continues to pose therapeutic challenges, tocilizumab maintains relatively stable efficacy across varying BMI ranges. Studies have demonstrated that obese individuals treated with tocilizumab exhibit a less pronounced reduction in therapeutic response when compared to their counterparts receiving TNF inhibitors [26]. A systematic review similarly noted reduced remission rates in patients receiving TNF inhibitors, but not in those treated with abatacept, rituximab, or tocilizumab [12].

In another study with a 48-week follow-up, obesity was found to have relations with a lower chance of a good treatment response, regardless of whether patients were treated with certolizumab-pegol, abatacept, or tocilizumab [23].

In our study, no significant association was discovered between the use of different b/tsDMARDs and disease activity in the overweight/obese group. This parallels findings from the Swiss SCQM registry (n=2,515), where DAS28-remission rates showed no BMI-dependent variations among adalimumab, etanercept, infliximab, and abatacept users [25]. This suggests that obesity/overweight is positively correlated with disease activity, irrespective of the type of pharmacologic therapy used, highlighting the need to consider baseline BMI as a potential stratification factor in future RA clinical trials. Additionally, our findings align with those of studies on psoriatic arthritis (PsA) and RA patients, where substantial weight loss, regardless of treatment, was associated with enhancements in disease activity [27].

The number of studies investigating the relationship between response to tsDMARDs and obesity remains quite limited. In the study investigating the efficacy of tofacitinib in patients with RA, Dikranian et al. [28] stratified RA patients into three groups based on BMI. Tofacitinib exhibited consistent efficacy across all three groups. In the study conducted by Novella-Navarro et al. [29], RA patients were analyzed in two groups, similar to our study. They did not identify any association between obesity and low disease activity in patients receiving JAK inhibitors. Unlike previous studies, the present study compared different biological pathways and tsDMARDs in RA patients. The BMI values, disease activity, and remission rates were found to be similar across the various treatment groups.

One of the key discoveries of the current study is that consistent patterns of switching between b/tsDMARDs across different BMI categories. This may support evidence that obesity does not significantly influence treatment cycle decisions in RA management. A Korean study on non-TNF-targeted therapies also found no BMI-related differences in drug persistence rates [30]. While obesity increases systemic inflammation, its effect on b/tsDMARDs durability seems to be minimized by current treatment strategies. Similarly, Japanese research showed that 1-year continuation rates for non-TNF inhibitors were the same regardless

of BMI [31]. These findings challenge the assumption that obesity requires different biologic treatment approaches.

In our study, the cumulative steroid dose did not differ between overweight/obese patients and those with a normal BMI. This aligns with findings from a German study, which also showed no association between glucocorticoid doses and BMI [20]. Similarly, another study on RA patients receiving both prednisolone and placebo reported no significant differences in body weight changes after two years [32]. Based on our results, the relationship between obesity and steroid use warrants reconsideration.

Despite these associations, obesity was not found to correlate with global patient assessments, tender joint counts, swollen joint counts, or fibromyalgia subgroup scores. This discrepancy highlights the complexity of the interplay between obesity, inflammation, and clinical manifestations of RA. Comparable clinical outcomes observed in both non-obese and obese RA patients underscore the importance of developing individualized therapeutic approaches.

This study's strengths lie in its robust analysis of the effect of obesity and being overweight on RA patients treated with both biologic and targeted synthetic DMARDs. Utilizing real-world information from a large cohort, it provides critical insights into treatment outcomes and glucocorticoid use, emphasizing obesity's broader implications in RA management.

In conclusion, while obesity/overweight is related to heightened disease activity and systemic inflammation in RA, its effect on the choice and switch rates of biologic and targeted synthetic treatments appears minimal. The similar clinical outcomes between obese/overweight and non-obese RA patients present an intriguing paradox, underscoring the complexity of RA management in the context of obesity. Nevertheless, managing obesity remains essential for improving overall health outcomes and potentially enhancing treatment responses in RA patients. Further research is warranted to fully elucidate the relationship between obesity, inflammation, and treatment efficacy in RA.

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Declarations

Conflict of interest The authors have no competing interests for this study.

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