

Prevalence of different types of surgery in rheumatoid arthritis patients: A study based on registry data of Rheumatology Clinic, Rafsanjan 2022

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Rheumatoid arthritis (RA) is a chronic systemic autoimmune disease that can affect many organs, and due to its systemic nature, it seems that some types of surgeries are more prevalent in this disease. This study aimed to investigate the prevalence of different types of surgery in RA patients. This retrospective study using the RA registry was performed on 639 RA patients in the rheumatology clinic of Rafsanjan, Iran, 2022. All patients fulfilled the ACR/EULAR 2010 classification criteria for RA. Demographic information, clinical parameters, laboratory information, surgical history, and surgery time were collected from the medical records. The sample comprises 555 (86.9%) women and 84 (13.1%) men. The average age was 55.08 ± 12.52 , and the mean duration of the disease was 7.32 ± 5.94 . There was a history of at least one surgery in 252 (39.4%) patients. The prevalence of gastrointestinal, gynecological, orthopedic, eye, ear, nose, and throat, cardiovascular and urological surgeries was 18%, 16.4%, 9.2%, 8.3%, 3.9%, 0.9% and 0.9%, respectively. There were 69.8% of eye surgeries and 57.6% of orthopedic surgeries after disease diagnosis; other surgeries were more prevalent before the diagnosis. The average age (58.16 ± 11.89 vs. 53.07 ± 12.53 , P-value < 0.001) and body mass index (29.65 ± 5.68 vs 28.63 ± 5.56 , P-value= 0.025) were higher in participants with surgery than those with no surgery. The most prevalent surgeries were gastrointestinal, gynecological, and orthopedic surgeries, and Cardiovascular and urological surgeries were the least. The mean age and body mass index in patients with surgery were significantly higher than those without surgery. Also, physical activity was significantly lower in the participants with surgery.

Keywords: rheumatoid arthritis; surgery; prevalence; orthopedic procedures

Introduction

Rheumatoid arthritis (RA) is a chronic and systemic disease with an inflammatory and autoimmune nature [1] that generally affects women more than men [2]. According to a

meta-analysis in 2020 [3], the global prevalence of RA was reported to be approximately 0.46% in the last 40 years. In 2008, the prevalence of this disease in Iran was 0.37% [4]. RA usually leads to symmetrical polyarthritis and generally

affects the small joints [5], and due to inflammation and hyperplasia of the synovium, it can destroy cartilage and soft tissue around the joint, including ligaments, tendons, and bone erosion [6-8]. All these can lead to joint destruction, loss of joint function, and disability [9, 10]. Patients who do not respond well to medical treatment are candidates for orthopedic surgeries [11]. Although the need for this type of procedure has decreased over the past decades due to progress in disease control [9, 12, 13], orthopedic procedures are still one of the most critical and common surgeries among these patients [7, 10, 14]. In addition, joint involvement and polyarthritis are not the only manifestations of RA; this disease also has extra-articular manifestations [15]. More than 35% of RA patients experience extra-articular manifestations [8]. Skin, oral mucosa, neurological, cardiovascular, pulmonary, gastrointestinal tract, hematologic, and almost every other organ system can be affected by RA with a wide range of clinical manifestations [8, 16, 17]. Since and due to systemic inflammatory processes and responses, some studies have shown a higher risk of some surgeries in RA [18-23]. Tzeng et al. 2015 showed a positive association between append-ectomy and RA [19], while some other studies have reported no significant relationship between appendectomy and RA [24, 25]. On the other hand, an investigation by Eftekharian in Iran indicated an inverse association between appendectomy and the risk of RA [26]. In addition, some studies have shown that coronary artery bypass grafting (CABG) is performed more frequently in RA patients than in the general population [18, 23]. In contrast with these studies, another investigation indicated that the prevalence of CABG was lower in RA patients because, despite the higher risk of cardiovascular disease in RA, these patients reported less angina and had a higher risk of sudden death [27]. Furthermore, a Canadian study reported increased cesarean section and obstetrical morbidity in RA patients [20].

Since various studies have reported that some types of surgeries are more common in RA

patients, and since no study has been conducted to determine the prevalence of different types of surgery in these patients, this study was conducted to determine the frequency of surgery in RA patients referred to Rafsanjan Rheumatology Clinic in 2011.

Materials and Methods

Study Design and Setting

This was a retrospective study using the data of the RA registry in the rheumatology clinic of Rafsanjan, Iran, 2022. The participants were selected based on the number of RA patients referred to the only rheumatology clinic in Rafsanjan. This study included 639 patients selected by census method. All the participants met the American College of Rheumatology/ European League Against Rheumatism (ACR/ EULAR) 2010 classification criteria for RA [28] and were diagnosed by a rheumatologist. Patients were excluded from the study in case of pregnancy, malignancy, cognitive disorders, or unwillingness to continue cooperation.

Data collection

Using a validated and pre-tested questionnaire, a trained interviewer collected the surgical history of participants and the surgery time. The questionnaire also included questions about patients' demographic data, history of other diseases, physical activity, smoking, and opium use. Laboratory tests, including erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), rheumatoid factor (RF), and anti-cyclic citrullinated peptide (anti-CCP), were collected from medical records of patients for the RA registry. Weight and height were also collected from medical records to calculate each participant's body mass index (BMI) by dividing each patient's weight in kilograms by the square of height in meters. History of surgery was recorded by asking this question "Do you have a history of any surgery?" and the answer was yes or no. Based on the answer to this question, patients were categorized into two sub-groups, with or without surgery, and the other characteristics were compared. If yes, it was followed up by asking, "What type of surgery did you have?" The answers included eye

ENT, cardiovascular, gastrointestinal, orthopedic, urological, and gynecological surgeries. Orthopedic surgeries included articular surgeries such as joint replacement and peri-articular surgeries, including tendon repair. Fracture operations due to trauma were not counted. Eye surgeries included surgeries due to cataracts. The time of surgery was recorded by asking this question: "When did you have surgery?" The answer was before RA diagnosis or after RA diagnosis. History of other diseases was asked by these questions: "Do you have a history of hypertension (HTN), hypercholesterolemia, diabetes mellitus, and heart disease diagnosed by a physician?". Physical activity, opium consumption, and smoking were self-reported.

Disease activity was evaluated using the Disease activity score in 28 joints (DAS28-score). This score is a continuous measure used to evaluate disease activity [29] and combines information from the status of 28 joints (swelling and tenderness), acute phase reactants including ESR and CRP, and patients' self-perceived health status using a visual analog scale. DAS28-score less than 2.6 is defined as remission, 2.6-3.2 indicates low activity, 3.2-5.1 shows moderate disease activity, and greater than 5.1 suggests severe disease [29]. This study presented this score as mean \pm standard deviation (SD). The protocol of this study was approved by the ethics committee of Rafsanjan University of Medical Sciences (Code: IR.RUMS.REC.1401.070).

Statistical Analyses

Results were presented as mean \pm standard deviation (SD) for numeric variables, and were summarized by absolute frequencies and percentages for categorical variables. Numeric variables were compared using the independent two-sample t-test and categorical variables were compared using the chi-square test or Fisher's exact test. The Kolmogorov-Smirnov test was used to evaluate the normality of quantitative data distribution. All statistical analyses were performed using SPSS software version 26 (IBM SPSS Inc., Chicago, IL, USA). The significance level was considered less than or equal to 0.05.

Results

This study included 639 RA patients, including 555 women (86.9%) and 84 men (13.1%). [Table 1](#) shows the participants' demographic, clinical, and laboratory parameters. The mean age of the participants was 55.08 ± 12.52 , and the mean duration of the disease was 7.32 ± 5.94 years. Most of the participants were housekeepers and lived in urban areas. Among participants, 255 (39.9%) had HTN, 118 (18.5%) had diabetes mellitus (DM), and 312 (48.8%) had hypercholesterolemia ([Table 1](#)).

There were 252 (39.4%) patients with a history of at least one surgery and 387 (60.6%) patients with no history of any previous surgery. The mean age of patients with surgery history was significantly higher than those without (58.16 ± 11.89 vs 53.07 ± 12.53 , P-value < 0.001). Furthermore, there were statistically significant differences in physical activity (P-value = 0.015), BMI (P-value = 0.025), HTN (P-value < 0.001), DM (P-value = 0.029), cardiovascular disease (P-value = 0.018) and hypercholesterolemia (P-value = 0.036) between patients with surgery and those without surgery ([Table 1](#)).

[Table 2](#) gives the prevalence of different types of surgeries. Surgeries performed on the gastrointestinal tract (GIT) were the most frequent type of surgery, and 115 (18%) participants had a history of this type of surgery. The least prevalent surgeries were cardiovascular and urological surgeries, in which 6 (0.9%) patients had a history of these types of surgeries. [Table 3](#) depicts the frequency of different types of surgeries based on the time of disease diagnosis. Eye and orthopedic surgeries were more frequent after the disease diagnosis. There were 37 (69.8%) and 34 (57.6%) patients who had experienced eye and orthopedic surgeries after diagnosis, respectively.

Other types of surgeries were more prevalent before the diagnosis. [Table 4](#) illustrates the baseline characteristics of patients with and without orthopedic surgery. The mean age (58.16 ± 11.89 vs 53.07 ± 12.53 , P-value < 0.001) and BMI (29.65 ± 5.68 vs 28.63 ± 5.56 , P-value = 0.025) were significantly higher in those with orthopedic surgery history. Also, there were significant differences in physical activity (P-

value = 0.037), occupation (P-value = 0.012), and HTN (P-value = 0.018). Based on this result, the frequency of low physical activity, having a

job as a housekeeper, and a history of HTN were significantly higher in those with orthopedic surgery history.

Table 1. Demographic, medical, and laboratory characteristics of study participants

Characteristics	Total (n=639)	No surgery history (n=387)	With surgery history (n=252)	P-Value
Gender-n (%)				0.219
Male	84 (13.1)	56 (14.5%)	28 (11.1%)	
Female	555 (86.9)	331 (85.5%)	224 (88.9%)	
Age (mean ± SD), year	55.08 ± 12.52	53.07 ± 12.53	58.16 ± 11.89	< 0.001
Education-n (%)				0.227
Illiterate	131 (20.5%)	71 (18.3%)	60 (23.8%)	
≤12 years	435 (68.1)	269 (69.6%)	166 (65.9%)	
≥ 13 years	73 (11.4)	47 (12.1%)	26 (10.3%)	
Physical activity-n (%)				0.015
Low	222 (34.7)	118 (30.5%)	104 (41.3%)	
Moderate	386 (60.4)	251 (64.9%)	135 (53.6%)	
Heavy	31 (4.9)	18 (4.6%)	13 (5.1%)	
Marital status-n (%)				0.185
Single	13 (2)	6 (1.6%)		
Married	584 (91.4)	360 (93.0%)	224 (88.9%)	
Divorced/Widowed	42 (6.6)	21 (5.4%)	21 (8.3%)	
Occupation-n (%)				0.074
Housekeepers	529 (82.8)	310 (80.1%)	219 (86.9%)	
Manual workers	76 (11.9)	52 (13.4%)	24 (9.5%)	
Office workers	34 (5.3)	25 (6.5%)	9 (3.6%)	
Residence-n (%)				0.843
Urban	474 (74.2)	286 (73.9%)	188 (74.6%)	
rural	165 (25.8)	101 (26.1%)	64 (25.4%)	
Cigarette smoker-n (%)		26 (6.7%)	19 (7.5%)	0.692
Opium consumption-n (%)	39 (6.1)	22 (5.7%)	17 (6.7%)	0.584
BMI (mean ± SD)	29.03 ± 5.63	28.63 ± 5.56	29.65 ± 5.68	0.025
Baseline co morbidity-n (%)	634 (99.2)	383 (99.0%)	251 (99.6%)	0.653*
Hypertension -n (%)				< 0.001
No	384 (62.1)	254 (65.6%)	130 (51.6%)	
yes	255 (39.9)	133 (34.4%)	122 (48.4%)	
Diabetes-n (%)				0.029
No	521(81.5)	326 (84.2%)	195 (77.4%)	
yes	118 (18.5)	61 (15.8%)	57 (22.6%)	
Hypercholesterolemia-n (%)				0.036
No	327 (51.2)	211 (54.5%)	116 (46.0%)	
yes	312 (48.8)	176 (45.5%)	166 (54.0%)	
Cardiovascular disease-n (%)				0.018
No	630(98.6%)	385(99.5%)	245(97.2%)	
yes		2(0.5%)	7(2.8%)	
Anti-CCP -n (%)				0.812
Negative	331 (51.8)	199 (51.4%)	132 (52.4%)	
positive	308 (48.2)	188 (48.6%)	120 (47.6%)	
CRP-n (%)				0.156
Negative	366 (57.3)	213 (55.0%)	153 (60.7%)	
positive	273 (42.7)	174 (45.0%)	99 (39.3%)	
Rheumatoid factor -n (%)		39 (51.3%)	16 (47.1%)	0.680
ESR (mean ± SD)	22.62 ± 17.74	22.79 ± 17.97	22.35 ± 17.42	0.775
DAS-score (mean ± SD)	3.92 ± 1.07	3.92 ± 1.06	3.92 ± 1.09	0.991
Duration of the disease (mean ± SD)	7.32 ± 5.94	7.18 ± 5.68	7.55 ± 6.32	0.450

BMI, Body mass index; anti-CCP, anti-cyclic citrullinated peptide; CRP, c-reactive protein; ESR, erythrocyte sedimentation rate; DAS, disease activity score

P-values were calculated by chi-square test

*P-value calculated by Fisher's exact test

Table 2: Prevalence of different types of surgeries

Types of surgery	No surgery history	With surgery history
Eye surgeries-n (%)	586 (91.7)	53 (8.3)
ENT surgeries-n (%)	614 (96.1)	25 (3.9)
Cardiovascular surgeries-n (%)	633 (99.1)	6 (0.9)
GI tract surgeries-n (%)	524 (82)	115 (18)
Orthopedic surgeries-n (%)	580 (90.8)	59 (9.2)
Urological surgeries-n (%)	633 (99.1)	6 (0.9)
Gynecological surgeries-n (%)	534 (83.6)	105 (16.4)
Any surgery history-n (%)	387 (60.6)	252 (39.4)

ENT, ear, nose, and throat; GI, gastrointestinal

Table 3: Prevalence of different surgeries based on the time of disease diagnosis

Types of surgery	Surgery before RA diagnosis	Surgery after RA diagnosis
Eye surgeries-n (%)	16 (30.2)	37 (69.8)
ENT surgeries-n (%)	18 (72)	7 (28)
Cardiovascular surgeries-n (%)	5 (83.3)	1 (16.7)
GI tract surgeries-n (%)	77 (66.96)	38 (33.04)
Orthopedic surgeries-n (%)	25 (42.4)	34 (57.6)
Urological surgeries-n (%)	5 (83.3)	1 (16.7)
Gynecological surgeries-n (%)	83 (79)	22 (21)

ENT, ear, nose, and throat; GI, gastrointestinal

Discussion

To the best of our knowledge, the present retrospective study was the first investigation to assess the prevalence of different types of surgery in RA patients. The prevalence of different surgeries in the patients of this investigation was as follows: 18% GI tract surgeries, 16.4% gynecological surgeries, 9.2% orthopedic

surgeries, 8.3% eye surgeries, 3.9% ENT surgeries and 0.9% for each cardiovascular and urological surgeries. There were 39.4% of patients who had experienced at least one surgery. Surgeries were more frequent before disease diagnosis except for eye and orthopedic surgeries. There were significant differences in mean age and BMI among patients with and without

surgery history and patients with and without a history of orthopedic surgery.

Table 4. Demographic, medical, and laboratory variables of patients with and without orthopedic surgery

Characteristics	No orthopedic surgery history (n=580)	With an orthopedic surgery history (n=59)	P-Value
Gender-n (%)			0.478
Male	78 (13.4%)	6 (10.2%)	
Female	502 (86.6%)	53 (89.8%)	
Age (mean ± SD)	54.48 ± 12.60	60.92 ± 10.09	< 0.001
Education-n (%)			0.498
Illiterate	118 (20.3%)	13 (22.0%)	
≤12 years	393 (67.8%)	42 (71.2%)	
≥ 13 years	69 (11.9%)	4 (6.8%)	
Physical activity-n (%)			0.037
Low	193 (33.3%)	29 (49.2%)	
Moderate	357 (61.6%)	29 (49.2%)	
Heavy	30 (5.1%)	1 (1.6%)	
Marital status-n (%)			0.075
Single	12 (2.1%)	1 (1.7%)	
Married	534 (92.1%)	50 (84.7%)	
Divorced/Widowed	34 (5.9%)	8 (13.6%)	
Occupation-n (%)			0.012
Housekeepers	472 (81.4%)	57 (96.6%)	
Manual workers	74 (12.8%)	2 (3.4%)	
Office workers	34 (5.9%)	0 (0)	
Residence-n (%)			0.582
Urban	432 (74.5%)	42 (71.2%)	
rural	148 (25.5%)	17 (28.8%)	
Cigarette smoking history-n (%)	41 (7.1%)	4 (6.8%)	0.934
Opium consumption-n (%)	37 (6.4%)	2 (3.4%)	0.361
BMI (mean ± SD)	28.83 ± 5.62	31.00 ± 5.31	0.005
Baseline co morbidity -n (%)	575 (99.1%)	59 (100.0%)	1.000*
Hypertension -n (%)			0.018
No	357 (61.6%)	27 (45.8%)	
yes	223 (38.4%)	32 (54.2%)	
Diabetes-n (%)			0.148
No	477 (82.2%)	44 (74.6%)	
yes	103 (17.8%)	15 (25.4%)	
Hypercholesterolemia-n (%)			0.383
No	300 (51.7%)	27 (45.8%)	
yes	280 (48.3%)	32 (54.2%)	
Cardiovascular disease-n (%)			0.845
No	572(98.6%)	58(98.3%)	
yes	8(1.4%)	1(1.7%)	
Anti-CCP -n (%)	283 (48.8%)	25 (42.4%)	0.347
CRP-n (%)	254 (43.8%)	19 (32.2%)	0.086
Rheumatoid factor -n (%)	50 (49.5%)	5 (55.6%)	1.000*
ESR -n (Mean ± SD)	22.83 ± 17.86	20.76 ± 16.73	0.409
DAS-score (mean ± SD)	3.90 ± 1.07	4.05 ± 1.00	0.316
Duration of the disease (mean ± SD)	7.13 ± 5.63	9.19 ± 8.21	0.065

BMI, Body mass index; anti-CCP, anti-cyclic citrullinated peptide; CRP, c-reactive protein; ESR, erythrocyte sedimentation rate; DAS, disease activity score

P-values were calculated by chi-square test; *P-value calculated by Fisher's exact test

In this investigation, the most prevalent type of surgery in patients was GIT surgery. Some studies demonstrated that some gastrointestinal surgeries, such as appendectomy, increase the risk of RA [19], while some other investigations were inconsistent with this finding [24-26]. Although, so far, no research has been done regarding the prevalence of gastrointestinal surgeries in these patients. The second most prevalent surgery in our study was gynecological surgery. This finding was consistent with other studies. A Canadian investigation [20], a nationwide population-based study in Taiwan [30], and another American study [31] revealed that cesarean section, as one of the gynecological surgeries, is a more prevalent and more frequent surgery in women with RA than unaffected women. Orthopedic surgery was the third most prevalent type of surgery in this study. Although orthopedic surgeries in RA patients have decreased in recent years due to improvements in disease control [32], these surgeries are still prevalent among these patients [7, 14]. Our findings also showed that the mean age of participants with orthopedic surgery was significantly higher than those without. This finding was consistent with a retrospective cohort study [33]. Furthermore, a significant increase in BMI was seen in patients with a history of orthopedic surgery. A cohort study by Richter et al [33] revealed that $BMI \geq 30 \text{ kg/m}^2$ was a risk factor for large joint surgeries. In contrast, another cohort study [34] did not mention $BMI \geq 30 \text{ kg/m}^2$ as a predictive factor for orthopedic surgeries among these patients. Another investigation also demonstrated that high BMI is associated with increased total knee arthroplasty in RA patients [35]. In addition, our results showed that the mean age and BMI of patients with any surgery history were higher than those without surgery.

Physical activity was lower in patients with a history of orthopedic surgery as well as in patients with any surgery history. Decreased physical activity can lead to obesity and high BMI [36], which can exacerbate the inflammatory process and destruction of joints, such as affected knees in RA patients. It can increase the risk of orthopedic surgeries [33, 35]. Furthermore, orthopedic surgeries were more

prevalent in housekeepers than the others in our study. No significant differences were seen in ESR and CRP, nor Anti-CCP and RF between participants with and without a history of orthopedic surgery in our study. There were different findings in various studies. A retrospective cohort study [34] has shown no significant effect of ESR, CRP, RF, and anti-CCP on orthopedic surgery. At the same time, some other investigations have demonstrated ESR [14, 37, 38] and CRP [37] as predictive factors for joint surgeries but did not mention RF and anti-CCP [14, 37, 38]. A possible reason for this inconsistency could be that the laboratory tests in our study were not baseline.

There was no significant difference in the DAS28 score between patients with and without surgery. This result was also observed between patients with a history of orthopedic surgery and those without orthopedic surgery. This finding did not align with the results of other studies that reported the association between DAS28-score and RA [38, 39]. This discrepancy may be due to the small sample size of our study. On the other hand, we do not know the basic DAS28 score in these patients, and it should be stated that some studies have shown the beneficial effect of orthopedic surgeries on the DAS28 score [40].

Cardiovascular and urologic surgeries were the least prevalent surgeries. Maradit-Kremers et al. [27], in 2005, revealed that RA patients are more likely to experience undiagnosed myocardial infarctions or sudden death due to lack of pain perception and absence of angina. Therefore, CABG in these patients is less prevalent compared to the general population. On the other hand, another investigation in 2021 demonstrated RA patients had a higher risk for cardiovascular disease, and CABG is a frequent and more prevalent surgery in these patients [18]. This incontinence might be due to the low prevalence of cardiovascular diseases in our study population and this issue can affect the results of CABG prevalence in the present study. There was no similar research regarding the prevalence of urological and other surgeries until now.

The main strength of this study was the use of registry information of almost all patients in the region. There were some limitations in our study.

First, the sample size was small. Second, the present investigation was only conducted on patients, and there was no control group. Third, we did not examine the drug history of the patients. It should also be mentioned that we did not have access to the reason for surgery in patients and their indications.

Conclusion

In this study, the most common type of surgery performed in RA patients was GIT surgery, followed by gynecological and orthopedic surgeries as the second and third most prevalent surgeries. The mean age and BMI in patients with a history of surgery were significantly higher than those without surgery. Also, physical activity was significantly lower in the group with a surgery history.

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Conflict of interest

The authors declare no conflict of interest.

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