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RESEARCH ARTICLE

A study to examine additional diabetes and cardiovascular risk variables and determine whether people on disease-modifying anti-rheumatic medications may be at varying risk for the disorder

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ABSTRACT

Objective and Aim: Rheumatoid arthritis patients are at risk for diabetes, which can result in a number of aftereffects and even cardiovascular disease, which is the leading cause of mortality for these individuals. According to earlier studies, certain rheumatoid arthritis medications may help stop diabetes from developing. The purpose of this study was to examine additional diabetes risk factors and determine whether people on disease-modifying anti-rheumatic medications (DMARDs) may be at varying risk for developing diabetes.

Materials & Methods: The analysis included 5530 adults without diabetes who had rheumatoid arthritis. An HbA1c score of ≥7% at follow-up was considered new-onset diabetes, which was the study's endpoint.

Result: When compared to Methotrexate monotherapy, the risk of diabetes was considerably lower during the bDMARD (HR 0.51; 95% CI 0.32 to 0.83), Methotrexate combination (HR 0.50; 95% CI 0.32 to 0.78), and other cDMARD (HR 0.56; 95% CI 0.37 to 0.84) periods. According to individual drug analysis, hydroxychloroquine decreased the incidence of diabetes (HR 0.52; 95% CI 0.42 to 0.65). Inhibitors of tumor necrosis factor-α tended to be protective (HR 0.69; 95% CI 0.46 to 1.03).

Conclusion: Patients with rheumatoid arthritis may have different levels of risk of diabetes depending on the treatment options.

Keywords: Diabetes, Rheumatoid arthritis, DMARDs, cardiovascular risk.

Introduction

Cardiovascular disease is more common in people with systemic inflammatory disorders[1–3]. An increase in cardiovascular risk factors also contributes to this excess risk, even if some of it is related to the direct effects of inflammation on the formation of atherosclerosis[4–8]. Furthermore, diabetes mellitus (DM) and other cardiovascular risk factors are probably accelerated by inflammation[9, 10]. Through a number of pathways, inflammation can lead to insulin resistance and diabetes mellitus. Insulin function appears to be blocked at the receptor level by tumor necrosis factor α (TNF-α) and interleukin (IL) 6; plasminogen activator inhibitor-1 and C-reactive protein are also negatively linked to insulin sensitivity[11–14]. Psoriasis and rheumatoid arthritis (RA), two prevalent systemic inflammatory diseases, put people at risk for diabetes mellitus and insulin resistance[15–17]. TNF inhibitors and other disease-modifying antirheumatic medications (DMARDs), which target the inflammatory response, are used to treat psoriasis and RA. Given the link between these disorders and DM, systemic immunosuppression may also lower the chance of developing DM. Evidence from epidemiological and interventional research supports this theory. Insulin resistance is improved by TNF inhibitors, according to several long-term studies[18, 19]. Anakinra, an IL-1 receptor antagonist, was reported to dramatically lower glycated hemoglobin levels in patients with type 2 diabetes in a small randomized controlled experiment[20]. Additionally, hydroxychloroquine, a DMARD approved by the US Food and Drug Administration (FDA) for the treatment of RA, was linked to a lower incidence of incident DM in a large observational research in a cohort of RA patients[21].

There are currently a number of strategies that may help RA patients avoid developing diabetes. Similar to the general population, obesity is one of the biggest risk factors for developing diabetes mellitus in RA patients. Another aspect that needs to be managed is RA disease activity, in addition to body weight. Studies have examined whether specific immunosuppressants have extra benefits in preventing DM in addition to the overall disease activity. For instance, a prior US cohort research identified abatacept, and another study indicated that inhibitors of tumor necrosis factor (TNF)-α may have protective effects[22]. Nevertheless, several investigations continue to fail to demonstrate the protective impact of biologics as described above[23-26].

As a result, the outcomes of these researches seem to be inconsistent with respect to the protective biologics. It's unclear if traditional disease-modifying anti-rheumatic medications (bDMARDs or cDMARDs, respectively) or other biologics would have comparable protective effects. We postulated that patients with RA might be shielded against developing DM by more potent DMARDs. To better understand the risk of DM in RA patients on various immunological medications, we therefore created a sizable cohort study.

Materials and Methods

Data Source and Patient Inclusion: Using the medical record database of the relevant clinics, which contains both inpatient and outpatient data that is often taken from the patient's original medical records, we created this retrospective cohort study.

Between January 2018 and December 2024, we found 3500 people who had been diagnosed with RA based on the International Classification of Diseases. 40 patients under the age of 20 were disqualified in accordance with the Institutional Review Board's guidelines. Furthermore, 210 patients who had diabetes mellitus prior to a diagnosis of RA were eliminated. The analysis included 3250 adult RA patients without diabetes mellitus. Following a modification in DMARD medication, incident DM was identified in certain subjects who had been diagnosed with RA or psoriasis. Using Cox proportional hazards regression, the RR of DM was calculated for TNF inhibitors, methotrexate, and hydroxychloroquine in comparison to other DMARDs. The Partners Healthcare institutional review board accepted the study methodology, and the need for patient consent was not required.

Study design: The day RA was diagnosed was designated as the index date. Every follow-up month, information about the pharmaceuticals of interest was taken out and updated. The definition of a prescription for the medicine of interest was one that was written within the month of the individual follow-up. We did not limit the number of fills, days, or doses because the data unit was one month; in other words, no minimal exposure to the medicine was necessary. It's unclear how long a medication will continue to influence the onset of diabetes mellitus after it has been stopped. To give a ballpark estimate, we take the time after stopping a medication and divide it by three half-lives. Here, we refer to this as the "washout period." A DM episode will be deemed drug-related if it happens during the washout time following the last prescription. It has been chosen to round up and set the washout period to one month if the drug's washout period is less than that because the data unit being referred to is measured in months. All forms of cDMARDs[27], tofacitinib[28], baricitinib[28], and etanercept[29] had a one-month medication washout time. If the washout period falls between 1 and 2 months, it has been determined to place it at the longer duration of 2 months. Abatacept[30], adalimumab[31], certolizumab[32], golimumab[33], and tocilizumab[34] all had a two-month medication washout time. Rituximab[35] had a six-month medication washout time.

Covariates and outcomes: Comorbidities included conditions like hypertension, hyperlipidemia, gout, chronic renal disease, hepatitis B and hepatitis C virus infection, coronary heart disease, and stroke that may be linked to RA therapies and DM risks. When RA was diagnosed, comorbidity was noted, and over the follow-up period, the status was updated. We identified the drugs, such as statins and steroids, that may be linked to the development of diabetes mellitus. Information on steroids and statins was updated during the follow-up period, much like the usage of DMARDs. Additionally, we retrieved laboratory data from the time of RA diagnosis, including hemoglobin, white cell count, and ten other measurements. New-onset diabetes mellitus, as indicated by a HbA1c value of ≥7% during follow-up, was the study endpoint. The patient was monitored at the individual clinics from the day of the RA diagnosis to the day of the DM diagnosis and the final appointment.

Statistical Analysis: Using an independent sample t-test for continuous factors or an X2 test for categorical variables, we examined the baseline characteristics at RA diagnosis (demographics, comorbidities, laboratory data, and medications) of patients with RA who had and did not have future incident DM. A time-dependent Cox proportional hazard model was used to compare the risk of incident DM under various treatment combinations pairwise. A rigorous SE was used to examine the outcome reliance of several follow-up months for a single patient. In the multivariable Cox model, we controlled for a number of established risk variables for diabetes mellitus, such as age, sex, body mass index (BMI, grouping), smoking, alcohol use, all comorbidities (time dependent), and time-dependent use of steroids and statins. SAS statistical software version 9.2 (SAS Institute Inc., Cary, North Carolina) was used for all statistical analyses.

Results

This study comprised a total of 3250 adult RA patients. With an incidence of 11.6 occurrences per 1000 PYs (95% CI 10.6 to 12.6), 320 patients (9.9%) developed DM throughout the course of the mean follow-up period of 9.2±5.6 years. Table 1 compares the baseline characteristics of RA patients with and without a future incidence of diabetes mellitus. Those with future incident DM were older, had higher BMI values, were more likely to be prescribed statins, had higher white cell counts, lower estimated glomerular filtration rate, higher C reactive protein levels, and more rheumatoid factor positivity ($p<0.05$) than patients without DM. They also had higher prevalence's of hypertension, gout, and hepatitis C virus infection.

Table 1: Baseline features of RA patients based on whether they would get diabetes in the future.

Variables	Total (N=3250)	Incidence of Diabetes		P Value
		Yes (N=2930)	*No (N=320)*	
Age (Years)	55.7±13.8	55.4±14.1	58.6±10.7	<0.001
Female (%)	2582 (79%)	2330 (79%)	252 (78%)	0.468
BMI (Kg/m^2)				
<18 kg/m^2	340 (10%)	328 (11%)	12 (4%)	<0.001
18-25 kg/m^2	1890 (58%)	1755 (60%)	135 (42%	<0.001
25-30 kg/m^2	794 (24%)	694 (24%)	100 (31%)	<0.001
>30 kg/m^2	226 (7%)	185 (6%)	41 (13%)	<0.001
Smoking (N%)	285 (9%)	258 (9%)	27 (8%)	0.578
Alcoholic (N%)	144 (4%)	129 (4%)	15 (5%)	0.742
Laboratory data at the diagnosis of RA				
Haemoglobin (g/l)	118±18	118±18	120±18	0.078
Creatinine (mg/dl)	0.79 (0.63, 0.92)	0.78(0.62, 0.91)	0.80 (0.70, 1.00)	0.626
ALT (U/l)	21 (17, 28)	21 (17, 28)	21 (16, 27)	0.940
AST (U/l)	17 (12, 26)	17 (12, 26)	19 (14, 27)	0.687
CRP (mg/l)	13 (4, 44)	13 (3, 42)	18 (4, 75)	<0.001
ESR (mm/hr)	34 (17, 62)	34 (16, 62)	35 (18, 65)	0.311
RF	1577 (48%)	1405 (48%)	172	0.038
Anti-CCP Antibody	225 (7%)	197 (7%)	28 (9%)	0.910
RF or Anti-CCP Antibody	1637 (50%)	1455 (50%)	182 (57%)	0.046
Comorbidity				
Hypertension	480 (15%)	413 (14%)	67 (21%)	<0.001
Hyperlipidaemia	90 (3%)	78 (2%)	12 (4%)	0.073
Gout	146 (4%)	125 (4%)	21 (7%)	0.017
Chronic Kidney Disease	313 (10%)	277 (9%)	36 (11%)	0.169
Coronary Heart Disease	122 (4%)	110 (4%)	12 (4%)	0.239
Hepatitis B virus infection	178 (5%)	164 (6%)	14 (4%)	0.002
Hepatitis c virus infection	256 (8%)	220 (8%)	36 (11%)	1.000
Stroke	48 (1%)	44 (2%)	4 (1%)	0.719
Medication at the diagnosis of RA				
Steroids	1087 (33%)	987 (34%)	100 (31%)	0.131
Statins	42 (1%)	35 (1%)	7 (2%)	0.036

Data were presented as frequency (percentage), mean±SD or median (first quartile, third quartile).BMI=Body Mass Index; ALT, alanine aminotransferase; anti-CCP, anti-cyclic citrullinated peptide; AST, aspartate aminotransferase; CRP, C reactive protein; eGFR, estimated glomerular filtration rate; ESR, erythrocyte sedimentation rate; RF, rheumatoid factor.

Other factors, such as age, sex, BMI, smoking, alcohol use, hypertension, hyperlipidemia, gout, chronic kidney disease, chronic hepatitis B and C virus infections, coronary artery diseases, and stroke, were also examined as potential contributors to the development of diabetes mellitus in RA patients. According to the findings, a higher risk of developing diabetes mellitus was linked to advanced age (HR 1.02; 95%CI 1.01 to 1.03), male sex (HR 1.33; 95%CI 1.04 to 1.70), higher body mass index (BMI), hypertension (HR 1.89; 95%CI 1.55 to 2.31), hyperlipidemia (HR 2.09; 95% CI 1.42 to 3.06), and hepatitis C virus infection (HR 1.35; 95% CI 1.02 to 1.79). Sulfasalazine (SSZ) (HR 0.69; 95%CI 0.54 to 0.87) and hydroxychloroquine (HCQ) (HR 0.52; 95%CI 0.42 to 0.65) were linked to a lower risk of DM in the individual medication analysis, while TNF-α inhibitors (HR 0.69; 95%CI 0.46 to 1.03) seemed to be protective. No other bDMARD was linked to a lower risk of developing DM (HR 0.78; 95%CI 0.39 to 1.53). In contrast, a higher incidence of diabetes mellitus was associated with time-dependent steroid use (HR 2.18; 95% CI 1.74 to 2.72). (Table 2)

Table 2: Diabetes Mellitus Incidence Rates by DMARD Usage

Variables	Adjusted HR (95%CI)	P value
Age (Year)	1.02 (1.01 to 1.03)	<0.001
Male (N%)	1.33 (1.04 to 1.70	0.022
BMI (Kg/m^2)		
<18 kg/m^2	1.68 (1.05 to 2.69)	0.032
18-25 kg/m^2	2.38 (1.47 to 3.85)	<0.001
25-30 kg/m^2	3.30 (1.97 to 5.51)	<0.001
>30 kg/m^2	1.77 (1.04 to 2.99)	0.034
Smoking (N%)	0.93 (0.65 to 1.32)	0.669
Alcoholic (N%)	1.18 (0.77 to 1.79)	0.453
Comorbidity		
Hypertension	1.89 (1.55 to 2.31)	<0.001
Hyperlipidaemia	2.09 (1.42 to 3.06)	<0.001
Gout	1.03 (0.75 to 1.42)	0.837
Chronic Kidney Disease	1.06 (0.80 to 1.41)	0.676
Coronary Heart Disease	0.97 (0.75 to 1.26)	0.841
Hepatitis B virus infection	0.89 (0.59 to 1.34)	0.578
Hepatitis c virus infection	1.35 (1.02 to 1.79)	0.036
Stroke	0.72 (0.45 to 1.15)	0.167
Medication		
Methotrexate	0.88 (0.70 to 1.11)	0.287
Hydroxychloroquine	0.52 (0.42 to 0.65)	<0.001
Sulfasalazine	0.69 (0.54 to 0.87)	0.002
Leflunomide	0.79 (0.51 to 1.21)	0.284
TNF-α inhibitors*	0.69 (0.46 to 1.03)	0.067
Other bDMARDs†	0.78 (0.39 to 1.53)	0.467
Time-dependent use of steroid	2.18 (1.74 to 2.72)	<0.001
Time-dependent use of statin	0.96 (0.61 to 1.51)	0.844

**Etanercept, adalimumab, certolizumab and golimumab.*

†Abatacept, tofacitinib, baricitinib, tocilizumab and rituximab.

bDMARDs, biological disease-modifying anti-rheumatic drugs; TNF, tumour necrosis factor.

Table 3 displays a variety of RA and CVD-related characteristics for both the various DMARD groups and the whole study cohort. The comparison of these factors between a DMARD group and the rest of the study population is also displayed in this table. Significantly shorter RA duration ($p < 0.001$), a smaller proportion of patients with erosions ($p < 0.001$), and a larger proportion of diabetics ($p = 0.002$) were observed in the 'only MTX ever' group. Compared to the other patients, the 'only SSZ ever' group had a significantly lower number of erosive patients ($p = 0.03$). The 'only HCQ ever' group had a longer RA duration than the other groups ($p = 0.01$). The 'SSZ and HCQ ever' group had a higher rate of patients seeking medication for hypertension ($p < 0.001$). RA duration was longer ($p = 0.04$) and the proportion of erosive patients was higher ($p < 0.001$) in the 'MTX, SSZ, and HCQ ever' group.

Table 3: The risk factors for incident diabetes in rheumatoid arthritis (RA) patients

Groups	N(%)	RA related variables (p value)			CVD related risk factors (p value)		
		RA duration	Percentage RF	Percentage erosive	Percentage hypertension	Percentage diabetes	Percentage hypercholesterolemia
Entire group	3250(100%)	9	72	82	22	6	4
Never MTX, SSZ or HCQ	196 (6%)	12 (0.25)	68 (0.58)	70 (0.06)	24 (0.74)	11 (0.19)	10 (0.11)
Only MTX ever	270(8%)	5 (<0.001)[a]	61 (0.09)	57 (<0.001)[a]	12 (0.06)	16 (0.002)[a]	6 (0.77)
Only SSZ ever	435 (13%)	8 (0.29)	70 (0.65)	73 (0.03)[a]	26 (0.38)	2 (0.16)	9 (0.14)
Only HCQ ever	190 (6%)	12 (0.01)[a]	70 (0.77)	81 (0.85)	17 (0.46)	3 (0.42)	4 (0.96)
MTX and SSZ ever	1055 (33%)	9 (0.10)	75 (0.18)	85 (0.12)	22 (0.97)	6 (0.80)	1 (0.11)
MTX and HCQ ever	106 (3%)	10 (0.83)	75 (0.73)	80 (0.12)	22 (0.97)	6 (0.80)	1 (0.11)
SSZ and HCQ ever	207 (7%)	10 (0.39)	69 (0.74)	90 (0.20)	39 (<0.001)[a]	3 (0.36)	0 (0.35)
MTX, SSZ and HCQ ever	790 (24%)	10 (0.04)[a]	73 (0.63)	91 (<0.001)[a]	20 (0.56)	5 (0.48)	5 (0.90)

Comparison calculated using a Students' t-tests or Pearson's Chi-square tests, relative to the remainder of the population. [a]Significant. 'RA duration' is in years; 'Percentage RF' refers to positive test for IgM rheumatoid factor; 'Percentage erosive' refers to erosions on radiographs of hands and/or feet. CVD, cardiovascular disease; DMARD, disease modifying anti-rheumatic drug; HCQ, hydroxychloroquine; MTX, methotrexate; RA, rheumatoid arthritis; RF, rheumatoid factor; SSZ, sulfasalazine.

Table 4 displays the ORs for CVD determined for three models that compare the different DMARD groups to the RA patients who have never taken SSZ, HCQ, or MTX. The 'only MTX ever', 'MTX and SSZ ever', and 'MTX, SSZ and HCQ ever' groups obtained significant CVD risk reductions from the first model, which adjusted for age, gender, smoking ever, and RA duration.

Table 4: Odds ratios for cardiovascular disease

Groups	Model 1 OR (95 percent CI)	Model 2 OR (95 percent CI)	Model 3 OR (95 percent CI)
Never MTX, SSZ or HCQ (reference)	1.0	1.0	1.0
Only MTX ever	0.15 (0.04–0.67)[a]	0.46 (0.08–3.24)	0.12 (0.01–0.52)[a]
Only SSZ ever	0.41 (0.15–1.11)	0.32 (0.08–1.34)	0.38 (0.13–0.98)[a]
Only HCQ ever	0.56 (0.17–1.68)	0.46 (0.11–2.05)	0.48 (0.14–1.47)
MTX and SSZ ever	0.21 (0.07–0.52)[a]	0.25 (0.06–0.87)[a]	0.17 (0.07–0.44)[a]
MTX and HCQ ever	0.21 (0.05–1.18)	0.53 (0.07–3.68)	0.20 (0.03–1.03)
SSZ and HCQ ever	0.45 (0.13–1.42)	0.35 (0.06–2.17)	0.36 (0.12–1.25)
MTX, SSZ and HCQ ever	0.21 (0.07–0.55)[a]	0.28 (0.06–0.98)[a]	0.17 (0.07–0.44)[a]

Model 1: correcting for age, gender, smoking and rheumatoid arthritis duration. Model 2: identical to 'Model 1' plus correction for hypertension, diabetes and hypercholesterolemia. Model 3: identical to 'Model 1' plus correction for a positive rheumatoid factor test and erosions. [a]Significant. CI, confidence interval; HCQ, hydroxychloroquine; MTX, methotrexate; OR, odds ratio; SSZ, sulfasalazine.

Discussion

The risk of DM episodes is increased by RA[36]. Our research also demonstrated that the odds of developing diabetes mellitus vary among RA patients receiving different therapies. Compared to patients on MTX (Methotrexate) monotherapy, individuals on bDMARD or cDMARD combination therapy will experience fewer DM episodes. Inhibitors of TNF-α, SSZ (sulfasalazine), and HCQ (hydroxychloroquine) seem to provide more potential protection. Early selection of appropriate medications, such as bDMARDs or combination therapy with cDMARDs, should be taken into consideration, as cardiovascular events are the primary cause of morbidity in RA.

The higher incidence of DM in RA patients has been attributed to a number of variables. The increased disease activity in RA is one of the main hazards[37]. Insulin resistance and diabetes mellitus may result from systemic inflammatory processes brought on by RA. A higher incidence of diabetes mellitus is linked to a number of cytokines and chemokines, such as interleukin (IL)-1 and IL-6. As a result, DM may be prevented by aggressively controlling disease activity to lower these cytokine levels. Better management of disease activity may be the reason why more effective treatments, such as bDMARDs or a combination of cDMARDs, were more beneficial than MTX alone in the current trial.

The current study's follow-up throughout each of the non-DMARD periods revealed that the patients were not taking DMARDs during this time; instead, they were only taking glucocorticoids or painkillers. In contrast to the bDMARD or cDMARD combination therapy periods, we observed that these times had a noticeably higher chance of developing DM. During these times, glucocorticoids rather than conventional immunotherapy may be the main factor controlling RA inflammation. Conversely, the glucocorticoid-sparing effects of bDMARD or cDMARD combination therapy may be responsible for the DM-preventive effects. The prevalence of glucocorticoid use in the current study was 8.4% during the DMARD period and 76.3% during the non-DMARD period. Long-term use of glucocorticoids increases gluconeogenesis in the liver while inhibiting the insulin response in skeletal muscle and adipose tissue decreases glucose uptake and utilization[38]. It also changes the composition of the body, including the growth of adipose tissue depots in the trunk, which leads to insulin resistance[39]. Therefore, according to the American College of Rheumatology and the European Alliance of Associations for Rheumatology, long-term glucocorticoid treatment is not advised[40,41].

There is a lack of research on the mechanisms via which DMARD use may affect the risk for CVD. According to reports, HCQ reduces total cholesterol

levels, which in turn affects cardiovascular risk[42-45]. Insulin resistance, hyperglycemia, weight gain, fluid retention, and hypertension are all documented side effects of corticosteroids that are linked to an elevated risk of cardiovascular disease[46]. MTX use may result in a folic acid shortage, which raises homocysteine levels and raises the risk of CVD[43, 47]. However, Choi and colleagues[44] found that MTX users with RA had a decreased cardiovascular mortality rate, which they attributed to the medication's anti-inflammatory properties. Choi and colleagues' findings of lower CVD-related mortality in patients treated with MTX are consistent with the decrease in CVD-related morbidity in these individuals. The current study's findings support the idea that lowering inflammation is crucial for lowering the risk of CVD by indicating that the usage of other traditional DMARDs, such as SSZ (although not notably HCQ), is also linked to a lower risk of getting CVD. The finding that joint damage and rheumatoid factor positive are linked to cardiovascular disease further emphasizes the link between inflammation and cardiovascular risk.

According to this study, using SSZ and HCQ seemed to lower the incidence of DM. According to earlier studies, HCQ users have noticeably decreased blood sugar levels[48]. An increase in adiponectin levels and insulin sensitivity may be the mechanism by which it has an anti-diabetic effect. While SSZ was also found to lower HbA1c, this could be because of a reduction in hemolysis rather than a true drop in glucose levels[49]. Since DM was defined in this study as HbA1c >7, some SSZ-treated patients might not be classified as having DM because of the aforementioned side effects. As a result, we can think that SSZ has a protective effect while, in reality, it might not exist.

In order to improve cardiovascular outcomes and lower early mortality, people with RA should pay close attention to DM prevention. Therefore, a number of factors need to be emphasized in addition to the medication options that were discussed in the current study, which may be beneficial. Since RA may also have an impact on other factors, controlling disease activity in RA is still crucial. Avoiding excessively static lifestyles is advised since they may be linked to joint abnormalities, weariness, or pain from RA. A patient who is able to move freely may find it easier to control their weight. Another risk factor for elevated inflammatory activity is body weight 50. In addition to body weight, individuals with rheumatoid arthritis should have routine DM screenings and lead healthy lifestyles to lower their chance of developing DM.

This study did have certain drawbacks, though. First, there might be missing data on patients with diabetes mellitus (DM) who had been stabilized in other facilities but were misdiagnosed as having no DM due to normal HbA1c readings. As an alternative, patients who were getting treatment in multiple medical facilities but were not on DMARDs were included in the periods. There may be a misclassification of treatment exposure (DMARD) and result (as determined by the HbA1c level). The study's findings will be impacted by these possibilities. Second, actual disease activity is not provided by this database retrospective study. Disease activity, however, could skew the drug's efficacy and impact the outcomes.

Conclusion

Compared to MTX alone, bDMARDs and DMARD combinations are more likely to lower the risk of DM in RA patients. While bDMARDs with alternative modes of action have demonstrated no impact, presumably because they are underutilized, HCQ and TNF-α inhibitors may have additional protective effects. Furthermore, long-term usage of steroids should be avoided due to their dose-dependent risk of DM episodes. Therefore, a wise treatment decision may help prevent future cardiovascular events and possibly help manage the development of diabetes mellitus in RA patients.

Data availability statement:

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author.

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Ethical Statement:

The study was conducted in accordance with the Declaration of Helsinki, and because it was retrospective in nature, the Institutional Review Board (IRB) waived the informed consent requirement.

Conflict of interest:

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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