J Rheum Dis 2024;31(4):212-222
https://doi.org/10.4078/jrd.2024.0026
pISSN: 2093-940X, eISSN: 2233-4718

Original Article

Anemia as an indicator of a higher retention rate for tocilizumab versus tumor necrosis factor inhibitors in patients with rheumatoid arthritis from a Korean multi-center registry

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Objective: To examine whether simple laboratory tests can guide selection between tocilizumab (TCZ) and tumor necrosis factor inhibitors (TNFi) in biologic-naive patients with rheumatoid arthritis (RA), by investigating their influence on drug retention.
Methods: Data of RA patients prescribed TCZ or TNFi as the initial biologics from March 2013 to December 2021 were obtained from the KOrean College of Rheumatology BIOlogics and Targeted Therapy (KOBIO) registry. Propensity score matching was performed to adjust for baseline confounding factors. Hazards of drug discontinuation for TCZ were calculated compared to those for TNFi. Interaction analyses with a Bonferroni-corrected p-value threshold were conducted to determine whether the hemoglobin level, C-reactive protein level, erythrocyte sedimentation rate, and platelet count affected the hazards of drug discontinuation.
Results: Overall, 893 patients were analyzed, of whom 315 and 578 were treated with TCZ and TNFi, respectively. The hazards of drug discontinuation in all patients were lower for TCZ than for TNFi (hazard ratio [HR]: 0.53, 95% confidence interval [CI]: 0.44~0.66). Notably, only the presence of anemia indicated a significant interaction (p for interaction=0.010); the HRs for drug discontinuation were 0.41 (95% CI: 0.30~0.55) and 0.70 (95% CI: 0.53~0.92) in the anemic and non-anemic groups, respectively. In the anemic subgroup, biologics were discontinued because of a lack of efficacy in 35.0% of TNFi initiators and 7.4% of TCZ initiators.
Conclusion: The drug discontinuation rate in biologic-naïve patients with RA was significantly lower for TCZ than for TNFi, particularly in those with anemia.

Keywords: Rheumatoid arthritis, Tocilizumab, Tumor necrosis factor inhibitors, Anemia

INTRODUCTION

Rheumatoid arthritis (RA) is a chronic autoimmune disease characterized by joint inflammation and deformity [1]. Disease-modifying antirheumatic drugs (DMARDs) represent a class of medications that modify the disease processes of RA by resolving inflammation and preventing radiographic progression [1]. In cases of inadequate response to conventional synthetic (cs) DMARDs, the subsequent measure involves the use of one of the following four classes of biologic (b) DMARDs: tumor necrosis factor inhibitors (TNFi), interleukin-6 (IL-6) receptor inhibitors, selective modulators of T-cell co-stimulation,

Received February 27, 2024; **Revised** April 30, 2024; **Accepted** May 29, 2024, **Published online** June 14, 2024
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and B cell-depleting agents [2,3]. These bDMARDs exhibit comparable therapeutic efficacy, and current guidelines do not specifically recommend one bDMARD over another as the first choice [2,3]. Nevertheless, it is worth noting that a substantial proportion of RA patients unresponsive to bDMARDs with one mode of action can achieve successful treatment outcomes by switching to bDMARDs with a different mode of action [4]. Given the heterogeneous nature of mechanisms underlying the pathogenesis of RA among patients, an individualized approach is highly desirable to effectively manage RA [1].

IL-6, the signature pathogenic cytokine of RA, plays a crucial role in mediating pathogenic T-cell differentiation, autoantibody production, and acute phase reactant synthesis [5,6]. As a predictive biomarker, RA patients with high serum IL-6 levels tend to show a more favorable response to IL-6 receptor inhibitors than to TNFi or methotrexate [7]. However, measuring the serum IL-6 levels is often not feasible or practical in most hospitals.

Previous reports indicated that simple laboratory tests could reflect the cytokine activity under inflammatory conditions [8]. In particular, a comprehensive literature search revealed that IL-6 was associated with hemoglobin (Hb) and C-reactive protein (CRP) levels, erythrocyte sedimentation rate (ESR), and platelet count [9-14]. Such associations were substantiated by experimental evidence demonstrating causality and by descriptive correlational data obtained from RA patient samples. Experimental studies reported the following as the functions of IL-6: induction of anemia via the promotion of hepatic synthesis of hepcidin [9,10]; induction of the full spectrum of acute phase reactants, including CRP [11,12]; and stimulation of thrombocytosis by upregulating thrombopoietin expression and directly promoting megakaryocyte differentiation [13,14]. Furthermore, several studies showed the significant correlations of serum IL-6 levels with Hb and CRP levels, ESR, and platelet count in RA patients [15-18]. Considering the negative relationship between mRNA levels of IL-6 and TNF-α in the peripheral blood of patients with RA, Nakagawa et al. [19] proposed a novel scoring system that incorporated some of these laboratory markers for the identification of patients with RA who would respond better to tocilizumab (TCZ) than to TNFi. Despite the significant results of this study, further investigations are required to validate this concept and enhance the applicability of common laboratory markers for guiding the selection of bDMARDs.

Herein, we hypothesized that biologic-naive RA patients with anemia, elevated acute-phase reactant levels, or thrombocytosis would have a markedly lower risk of drug discontinuation for TCZ than for TNFi. Therefore, this study investigated whether the results of the aforementioned laboratory markers affected the hazards of drug discontinuation of TCZ relative to that of TNFi by examining their interaction.

MATERIALS AND METHODS

Study population and data source

The KOrean College of Rheumatology BIOlogics and Targeted Therapy (KOBIO) registry is an observational multicenter registry of Korean patients with RA, ankylosing spondylitis, and psoriatic arthritis who have newly initiated or switched to bDMARDs or targeted synthetic DMARDs (ClinicalTrials.gov identifier NCT01965132) [20]. RA patients met the 2010 American College of Rheumatology/European League Against Rheumatism criteria and were >18 years of age [21]. Demographic and clinical data, as well as information on laboratory results, functional status, and concomitant use of csDMARDs and corticosteroids, were collected upon enrollment and at subsequent yearly visits. Data on treatment discontinuation, including the reasons and dates, were also obtained during follow-up. All patients were managed at the discretion of attending physicians, who determined the choice of bDMARD and treatment maintenance.

The present study retrospectively analyzed data obtained from the KOBIO registry from March 2013 to December 2021. Only biologic-naïve RA patients who were initiated on either TCZ or TNFi (infliximab, adalimumab, etanercept, golimumab, or biosimilar infliximab) at the time of enrollment and who had at least one set of follow-up data with a follow-up duration of 1 year or longer were included in the study. Patients with missing data on the factors required for subsequent propensity score matching and the date of drug discontinuation were excluded from the analysis.

This study was conducted according to the principles of the Declaration of Helsinki. The study protocol and data collection forms were approved by the institutional review board of each participating center, including the Institutional Review Board of Inje University Ilsan Paik Hospital (ISPAIK 2013–04-116). Written informed consent was obtained from all the patients.

Data collection

Baseline (i.e., at the time of initiating treatment with the first bDMARD) and annual follow-up data were extracted from the KOBIO registry database. Specifically, data on the following were obtained: age, sex, disease duration, smoking status, body mass index, comorbidities, swollen joint count, tender joint count, physicians' and patients' global assessment, Disease Activity Score in 28 Joints (DAS28) with ESR and CRP, Clinical Disease Activity Index (CDAI), Simplified Disease Activity Index (SDAI), Routine Assessment of Patient Index Data 3 (RAPID3), and concomitant use of medications for RA, such as corticosteroids, methotrexate, leflunomide, sulfasalazine, hydroxychloroquine, tacrolimus, bucillamine, mizoribine, azathioprine, and cyclosporine. Laboratory data, including ESR, CRP, Hb, white blood cell count, platelet count, rheumatoid factor (RF), and anti-citrullinated protein antibody (ACPA), were extracted. Information regarding the presence of erosion on plain radiographs and regarding the dates of both bDMARD initiation and discontinuation were also obtained. Data on the reasons for the discontinuation of bDMARDs, including a lack of drug efficacy, adverse events, clinical remission, and non-toxic causes (e.g., financial issues, preparing for pregnancy, and patients' unwillingness), were collected.

Statistical analysis

Propensity score matching was performed at a 1:2 ratio to adjust for baseline confounding factors between TCZ and TNFi initiators. The following covariates were chosen based on ex-

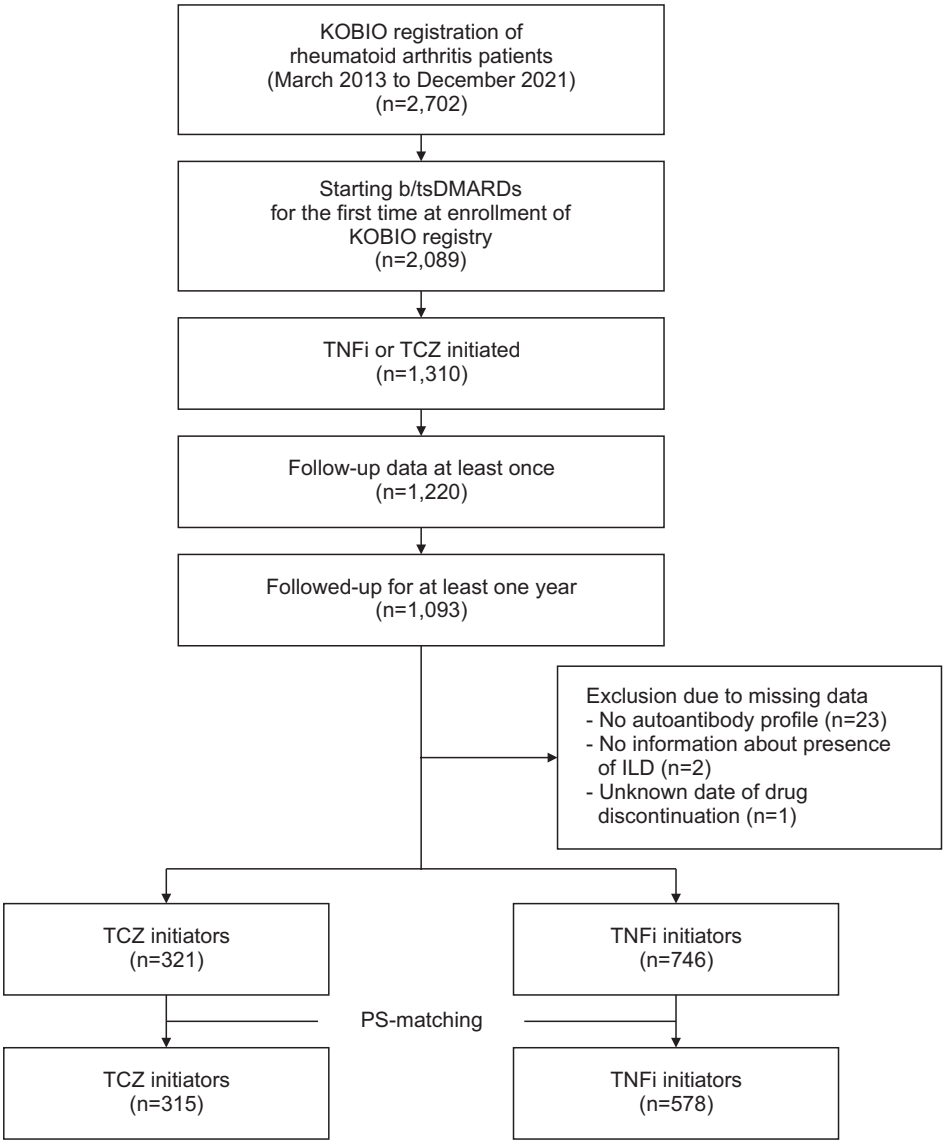

Figure 1. Patient selection process. KOBIO registry: Korean College of Rheumatology BIOlogics and Targeted Therapy Registry, b/tsDMARDs: biologic or targeted synthetic disease-modifying antirheumatic drugs, TCZ: tocilizumab, TNFi: tumor necrosis factor inhibitors, PS-matching: propensity score matching, ILD: interstitial lung disease.

pertise regarding their potential influence on bDMARD selection or effectiveness: age, sex, body mass index, RA duration, baseline CDAI, tender joint count, swollen joint count, RF or ACPA positivity, glucocorticoid use, methotrexate use, and presence of interstitial lung disease. With these covariates, a logistic regression model was constructed to calculate the propensity score, defined as the probability of starting TCZ or TNFi treatment. For this study, 1:2 nearest-neighbor matching within the range of propensity score calipers was employed, with the caliper width set at 0.2. After propensity score matching, baseline patient characteristics were presented as mean±standard deviation or frequency (percentage) with standardized difference. A standardized difference exceeding a threshold of 0.1 suggested a meaningful difference between the groups. Cox proportional hazards regression was used to determine hazard ratios (HRs) and 95% confidence intervals (CIs) of drug discontinuation of TCZ compared with that of TNFi from the initial prescription date of bDMARDs. Kaplan–Meier curves were plotted to visualize the temporal changes in drug retention rates. For interaction analyses, we selected Hb, CRP, ESR, and platelet count based on their known associations with IL-6 [9-14]. Binary cutoff values were set according to generally accepted references: anemia

Table 1. Baseline characteristics of propensity score-matched participants

	TNFi initiators (n=578)	TCZ initiators (n=315)	d
Female	480 (83.0)	262 (83.2)	0.003
Age (yr)	53.8±12.5	54.6±12.8	0.064
Disease duration (yr)	6.1±7.2	6.1±6.9	0.001
Body mass index (kg/m^2)	22.6±3.5	22.6±3.3	0.005
Smoking history			0.066
Ex-smoker	48 (8.3)	32 (10.2)	
Current smoker	37 (6.4)	21 (6.7)	
Never	493 (85.3)	262 (83.2)	
RF positivity	484 (84.6)	264 (84.1)	0.015
ACPA positivity	432 (85.4)	239 (83.3)	0.058
Hemoglobin (g/L)	120.6±13.3	119.8±14.5	0.061
White blood cell count (×10^9/L)	8.3±2.6	8.2±2.8	0.034
Platelet count (×10^9/L)	295.7±82.4	298.9±83.6	0.038
ESR (mm/hour)	48.6±27.5	46.0±28.0	0.096
CRP (mg/L)	21.1±23.8	24.0±29.2	0.109
Swollen joint count	6.41±5.09	6.50±5.05	0.017
Tender joint count	8.08±6.11	8.08±5.74	<0.001
DAS28-ESR	5.5±1.0	5.5±1.0	0.007
DAS28-CRP	4.8±1.0	4.9±1.0	0.085
SDAI	28.7±10.7	29.3±10.7	0.061
CDAI	26.6±10.2	26.9±10.1	0.029
RAPID3	15.4±5.2	15.6±5.8	0.033
Radiographic joint erosion	198 (39.5)	117 (42.2)	0.055
Interstitial lung disease	15 (2.6)	15 (4.8)	0.115
Concurrent use of csDMARDs	570 (98.6)	311 (98.7)	0.010
Number of csDMARDs	1.69±0.73	1.81±0.73	0.166
Concurrent use of methotrexate	552 (95.5)	295 (93.7)	0.082
Concurrent corticosteroid	511 (88.4)	276 (87.6)	0.024
Corticosteroid dose (dose equivalent for prednisolone in mg/day)	5.5±3.4	5.4±3.1	0.040

Values are presented as number (%) or mean±standard deviation. TNFi: tumor necrosis factor inhibitors, TCZ: tocilizumab, d: standardized difference, RF: rheumatoid factor, ACPA: anti-citrullinated protein antibody, ESR: erythrocyte sedimentation rate, CRP: C-reactive protein, DAS28: Disease Activity Score in 28 Joints, SDAI: Simple Disease Activity Index, CDAI: Clinical Disease Activity Index, RAPID3: Routine Assessment of Patient Index Data 3, csDMARDs: conventional synthetic disease-modifying antirheumatic drugs.

was defined as Hb <130 g/L for male patients and Hb <120 g/L for female patients [22]; CRP elevation was defined as CRP ≥10.0 mg/L [23]; abnormally elevated ESR was defined as ESR ≥28 mm/hour [24]; and thrombocytosis was defined as platelet count >450×10^9/L [25]. Subsequently, an interaction term was added to the Cox regression model to investigate whether each laboratory marker affected the hazards of drug discontinuation. All statistical analyses were performed using R software (version 4.3.0; R Foundation for Statistical Computing, Vienna, Austria) with statistical significance set at a p-value of <0.05. However, for interaction, a more stringent p-value cutoff of 0.0125 was applied with Bonferroni correction, calculated as 0.05 divided by 4 (the number of interaction analyses performed).

RESULTS

Baseline patient characteristics

The patient selection process is illustrated in Figure 1. A total of 746 TNFi initiators and 321 TCZ initiators were included as unmatched participants (Supplementary Table 1). Subsequently, 578 TNFi initiators and 315 TCZ initiators were analyzed after propensity score matching.

The baseline characteristics of matched RA patients are summarized in Table 1 and Supplementary Table 2. The mean age and proportion of females were similar. With respect to the clinical characteristics of RA, the two groups were similar in various domains, including disease duration, autoantibody profile, disease activity, functional index, and proportion of radiographic erosion. Medication profiles and comorbid conditions were similar between the two groups. However, in the TCZ group, more csDMARDs were concurrently prescribed (mean±SD: 1.69±0.73 vs. 1.81±0.73; d=0.166) and interstitial lung disease was more frequent (2.6% vs. 4.8%, d=0.115). Among the TNFi initiators, 221 (38.2%) received adalimumab, 147 (25.4%) received etanercept, 100 (17.3%) received biosimilar infliximab, 82 (14.2%) received golimumab, and 28 (4.8%) received originator infliximab. Certolizumab pegol was administered in none of the patients.

Comparison of drug retention rates between TCZ and TNFi in overall RA patients

The mean follow-up duration was 32.4±29.3 months for the TNFi group and 39.7±26.6 months for the TCZ group. In 362 (62.6%) patients in the TNFi group and 126 (40.0%) patients in the TCZ group, bDMARDs were discontinued during the follow-up period. Hazards of discontinuation were lower in TCZ initiators than in TNFi initiators (HR: 0.53, 95% CI: 0.44~0.66, p<0.001; Figure 2A). The percentage of cause-specific drug discontinuation among overall patients is illustrated in Figure 2B.

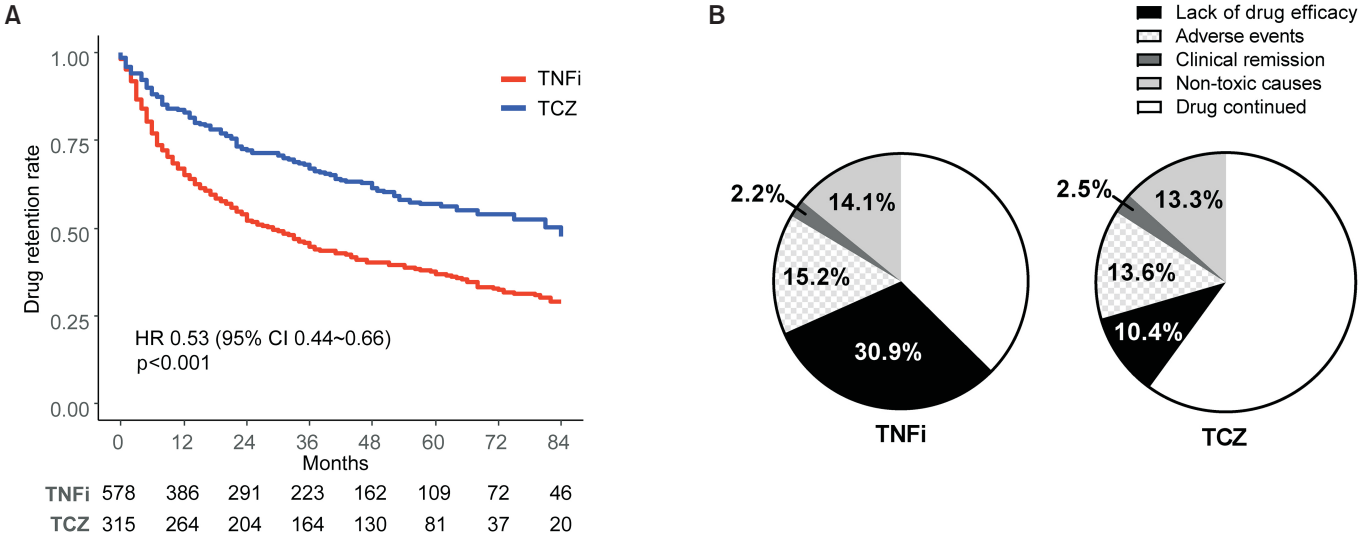

Figure 2. Comparison of drug retention rates between TCZ and TNFi in biologic-naïve RA patients. (A) Kaplan–Meier curves comparing drug retention rates between TCZ and TNFi initiators with the HR of drug discontinuation for TCZ versus TNFi. (B) Percentage of cause-specific drug discontinuation among total patients during the entire follow-up period. TCZ: tocilizumab, TNFi: tumor necrosis factor inhibitors, RA: rheumatoid arthritis, HR: hazard ratio, CI: confidence interval.

Interaction of laboratory markers with hazards of drug discontinuation

Next, interaction analyses were conducted to determine whether each selected laboratory marker affected hazards of discontinuation. Only the presence of anemia significantly affected hazards of TCZ discontinuation (versus TNFi discontinuation) (p=0.010); the interaction was not qualitative but quantitative (Figure 3). Given the significant interaction with the presence of anemia, Kaplan–Meier curves were plotted to compare drug-retention rates between TNFi and TCZ in subgroups with and without anemia (Figure 4A and 4B). In the anemic subgroup, the hazard of discontinuation was remarkably lower for TCZ than for TNFi (HR: 0.41, 95% CI: 0.30~0.55, p<0.001) (Figure 4A), whereas the non-anemic subgroup displayed a lesser degree of difference (HR: 0.70, 95% CI: 0.53~0.92, p=0.011) (Figure 4B). In the anemic subgroup, biologics were discontinued because of a lack of efficacy in 35.0% of TNFi initiators and 7.4% of TCZ initiators. (Figure 4C). In the non-anemic subgroup, biologics were discontinued because of a lack of efficacy in 26.7% of TNFi initiators and 13.7% of TCZ initiators (Figure 4D). To identify factors that may influence drug-retention rates, baseline patient characteristics for both anemic and non-anemic patients are summarized in Supplementary Tables 3 and 4. Significant differences were observed between TNFi and TCZ initiators, with the most notable differences as follows. In anemic participants, the TCZ group was prescribed a greater number of csDMARDs concurrently compared to the TNFi group (mean±SD: 1.70±0.73 vs. 1.91±0.73, d=0.295) (Supplementary Table 3). Among participants without anemia, interstitial lung disease was more frequent in the TCZ group than in the TNFi group (1.8% vs. 5.9%, d=0.216) (Supplementary Table 4).

DISCUSSION

The present study showed that, compared to TNFi, TCZ had superior retention rates in RA patients, with a notably enhanced retention rate for TCZ in the presence of anemia. We examined whether Hb, CRP, ESR, and platelet count affected the hazards of drug discontinuation for TCZ relative to TNFi using a Bonferroni-corrected p-value threshold; anemia was identified as the sole significant interactor. In the anemic subgroup, the hazards of discontinuation were remarkably lower for TCZ, whereas the non-anemic subgroup displayed a less marked difference. Notably, in the anemia subgroup, the proportion of discontinuation due to inadequate drug efficacy was 35.0% in the TNFi group and 7.4% in the TCZ group. While anemia has

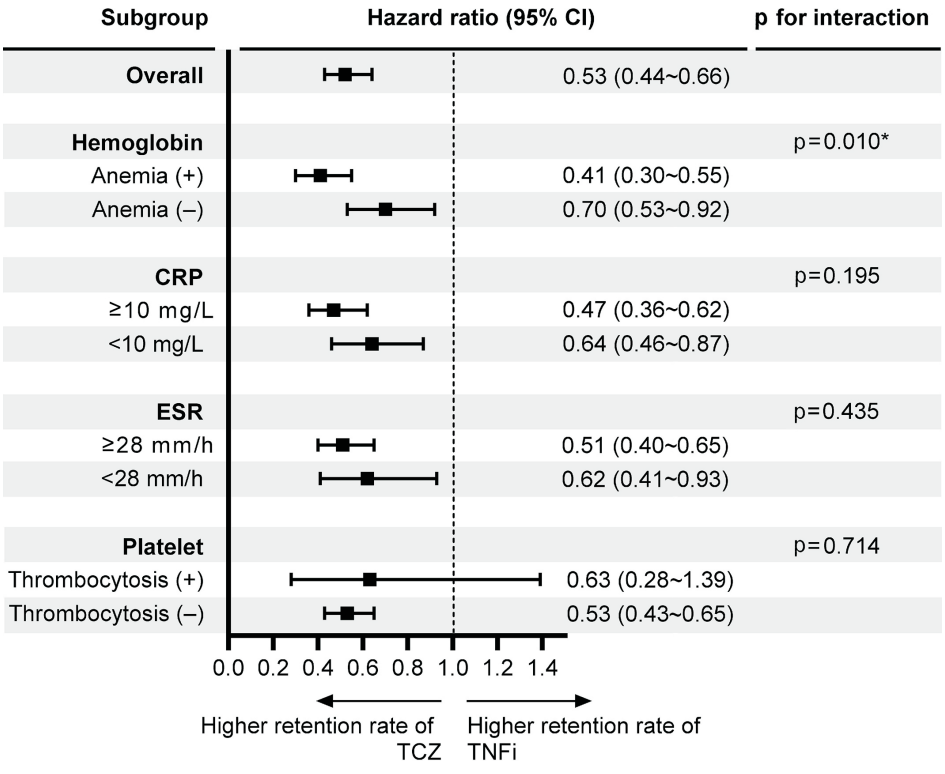

Figure 3. Cox regression analyses for the interaction between laboratory markers and choice of biologics. TCZ: tocilizumab, TNFi: tumor necrosis factor inhibitors, CRP: C-reactive protein, ESR: erythrocyte sedimentation rate, CI: confidence interval. *p for interaction <0.0125.

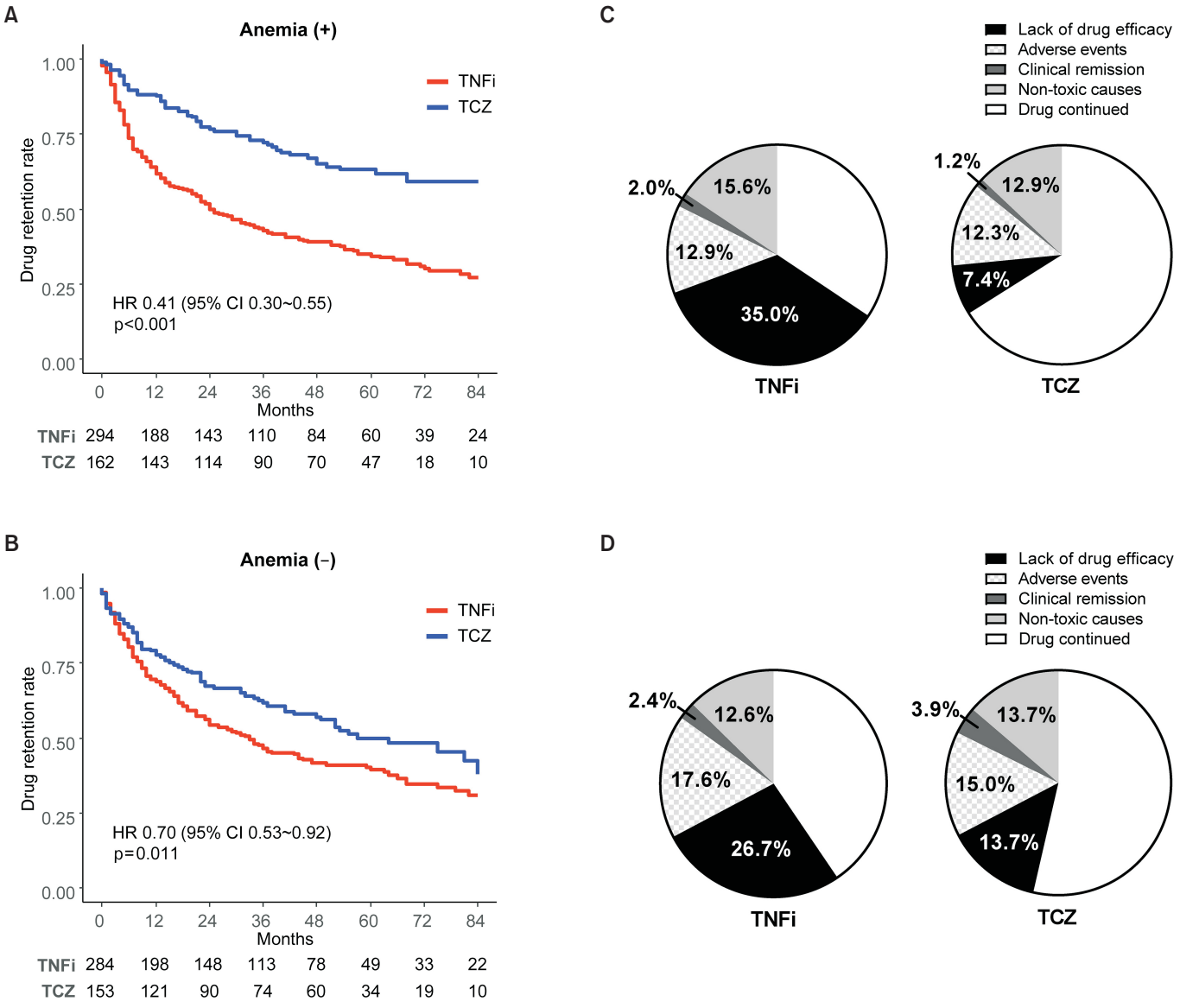

Figure 4. Comparison of drug retention rates between TCZ and TNFi in the subgroups with or without anemia. (A) Kaplan–Meier curves comparing the drug retention rates between TCZ and TNFi initiators with the HR of drug discontinuation for TCZ versus TNFi in anemic subgroup. (B) Kaplan–Meier curves comparing the drug retention rates between TCZ and TNFi initiators with the HR of drug discontinuation for TCZ versus TNFi in non-anemic subgroup. (C) Percentage of cause-specific drug discontinuation among anemic subgroups during the entire follow-up period. (D) Percentage of cause-specific drug discontinuation among non-anemic subgroups during the entire follow-up period. TCZ: tocilizumab, TNFi: tumor necrosis factor inhibitors, HR: hazard ratio, CI: confidence interval.

been previously recognized as a potential biomarker for bDMARD selection [19], we suggest its guiding role based on the drug retention rates using multicenter, long-term registry data. Our findings support the value of Hb as a simple and readily accessible biomarker for navigating initial bDMARD treatment in RA.

TCZ was associated with significantly higher drug retention than TNFi in patients with biologic-naïve RA. This finding is consistent with those of the previous studies. Multinational European cohort data have consistently suggested higher drug retention rates for TCZ than for TNFi in biologic-naive patients as well as in biologic-experienced patients [26,27]. Recent research has also demonstrated that anemic patients with RA exhibit higher drug retention rates for TCZ and Janus kinase inhibitors compared to those for other bDMARDs [28]. However, interpreting differences in drug retention rates between TNFi and TCZ should be done with caution owing to varied retention profiles among TNFi. For example, etanercept has the highest

retention rates, indicating that these differences may not be consistent across all TNFi [29]. Another point to note is that drug retention rates indicate both efficacy and safety, underscoring the need to understand why drugs are discontinued. Jinno et al. [30] found that patients with elderly-onset RA had a higher retention rate for IL-6 receptor inhibitors compared to that for TNFi, mainly owing to the lower efficacy of TNFi leading to discontinuation. Similarly, the proportion of bDMARDs halted owing to a lack of drug efficacy also differed in our analysis (30.9% for TNFi and 10.4% for TCZ) (Figure 2B).

In the present study, anemia significantly affected hazards of TCZ discontinuation (compared with TNFi discontinuation). In cases of anemia, the superior drug retention of TCZ compared to that of TNFi becomes even more pronounced. This is primarily due to the higher rate of drug discontinuation due to the lack of efficacy among TNFi initiators with anemia. Anemia is widely associated with IL-6 activity under chronic inflammatory conditions [10]. The biological mechanism of IL-6 involves the induction of hepatic synthesis of hepcidin, a regulator that impedes both intestinal iron absorption and release from the reticuloendothelial system [9,31,32]. Consequently, IL-6 leads to a reduction in the available iron pool and development of anemia. RA patients with anemia exhibited elevated serum IL-6 levels compared to RA patients without anemia [17], and administration of an IL-6 receptor inhibitor effectively restored their anemia and hepcidin levels [33]. Although anemia is influenced by a range of proinflammatory cytokines, including TNF-α [34,35], the role of TNF-α is less potent than that of IL-6 [17,33,36]. Strikingly, Nakagawa et al. [19] revealed that among various laboratory markers, pretreatment Hb levels in patients with RA exhibited the strongest negative correlation with improvement in DAS28 after treatment with TCZ. However, this correlation was not found in the group treated with TNFi [19]. Taken together, the presence of anemia in RA patients, primarily associated with IL-6 rather than TNF-α, suggests that using TCZ instead of TNFi when initiating biologic agents further improves drug retention.

In our analysis, the interaction of CRP elevation on HRs was not statistically significant. The subgroup with CRP elevation exhibited marginally lower hazards of TCZ discontinuation (versus TNFi discontinuation) than the subgroup without CRP elevation. A previous study reported that RA patients with elevated CRP levels had a higher retention rate for TCZ than for TNFi; however, an interaction analysis was not conducted in that study [37]. Other previous reports indicated that pretreatment CRP levels did not correlate with DAS28 improvement after TCZ initiation [19] and that baseline serum CRP levels were not predictive of TCZ response in RA patients [38]. Therefore, the modest outcome regarding the impact of CRP elevation is in line with prior data. Similarly, the ESR, which is an indirect measure of acute-phase reactants (including CRP) exhibited an interaction tendency similar to that of CRP.

The observation of the interaction of thrombocytosis contrasts with the findings of previous studies. As previously demonstrated, the initial platelet count was identified as being associated with subsequent improvement in DAS28 following TCZ initiation [19]. However, our current analysis revealed that HR increased in the presence of thrombocytosis compared to those without thrombocytosis. This unexpected finding could be attributed to the small number of patients with thrombocytosis, potentially introducing bias into the results and broadening the range of CIs. Consequently, it is difficult to draw conclusions regarding the impact of thrombocytosis in this study.

Previous studies indicated that IL-6 affects liver homeostasis [39]. The liver enzymes aspartate aminotransferase (AST) and alanine aminotransferase (ALT) are related to the TCZ response; however, these laboratory markers are subject to numerous confounding factors [19]. AST and ALT levels are notably influenced by concurrent medications for comorbidities, the amount of alcohol consumed, and the presence of fatty liver. Unfortunately, these crucial details were not obtained from the registry. Therefore, these markers were excluded from analysis.

Subgroup analysis is susceptible to the risk of type I errors, also known as false positives. This susceptibility arose from an increased number of analyses. To mitigate this risk and enhance the reliability of results, it is advisable to adhere to certain conditions. These include the use of specified variables and hypotheses, conducting interaction analyses, adjusting statistical thresholds, and validation with external cohort [40]. We selected Hb, CRP, ESR, and platelet count for analysis because there is a solid theoretical background explaining the association between these markers and IL-6. We hypothesized that RA patients with anemia, high CRP levels and ESR, or thrombocytosis would exhibit a more favorable response to TCZ than to TNFi. Thereafter, interaction analyses were performed, and the p-value threshold was adjusted to minimize the risk of type I errors.

This study had some limitations. First, external validation was not performed, necessitating further confirmation of the results.

Second, propensity score matching is a widely acknowledged statistical method for balancing two different patient groups in retrospective studies. However, this method selectively includes patients with similar intergroup characteristics, inadvertently excluding a particular spectrum of patients from the analysis. In addition, unnoticed imbalances between groups may exist even following the matching process. Third, anemia can result from various comorbidities and is not limited solely to IL-6 activity in RA. Chronic kidney disease, hematological malignancies, and solid tumors, all of which cause anemia, were prevalent in only 1.2%, 0.0%, and 0.1% of matched participants, respectively (Supplementary Table 2). Therefore, the applicability of our findings to individuals with anemia-related diseases other than RA remains unclear.

CONCLUSION

Biologic-naïve RA patients displayed a higher retention rate for TCZ than for TNFi. In anemic RA patients, TCZ was markedly superior to TNFi with respect to the drug retention rate, with the presence of anemia having a significant quantitative interaction. In the anemic subgroup, the reason for drug discontinuation was a lack of clinical efficacy in 35.0% and 7.4% of TNFi and TCZ initiators, respectively. Collectively, we suggest that TCZ might be a better option than TNFi in biologic-naïve RA patients, particularly in those with anemia.

FUNDING

None.

ACKNOWLEDGMENTS

We thank the medical staff at all the hospitals participating in the KOBIO registry for providing data. We express our sincere appreciation to all the members who contributed to the management of the registry data.

CONFLICT OF INTEREST

BSK has been an editorial board member since May 2022, but has no role in the decision to publish this article. The authors declare that they have no competing interests.

AUTHOR CONTRIBUTIONS

JGK and BYY contributed to the study conception and design. JGK contributed to data acquisition. All authors contributed to the analysis and/or interpretation of data. JGK, BSK, and BYY contributed to drafting the manuscript. JGK and JHL contributed to revising the manuscript. All authors reviewed and approved the final version of the manuscript.

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SUPPLEMENTARY DATA

Supplementary data can be found with this article online at https://doi.org/10.4078/jrd.2024.0026

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