CYTOKINE-GUIDED IMMUNOLOGICAL CORRECTION AFTER TOTAL KNEE ARTHROPLASTY IN RHEUMATOID ARTHRITIS: FIRST REAL-WORLD MULTICENTER STUDY FROM UZBEKISTAN

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Annotation

This multicenter real-world study from Uzbekistan evaluated cytokine-guided postoperative immunological correction in patients with rheumatoid arthritis undergoing total knee arthroplasty. A total of 106 patients were stratified according to dominant cytokine profiles, including TNF-α, IL-6, and IL-1β, and received pathway-matched biologic therapy with csDMARDs. Over 52 weeks, significant improvements were observed in DAS28, HAQ-DI, VAS pain, CRP, ESR, and cytokine levels. Nearly half of the patients achieved remission, and most reached low disease activity. No prosthetic joint infections, implant failures, or deaths were recorded. These findings suggest that cytokine-guided personalized therapy may improve postoperative recovery, disease control, and safety in rheumatoid arthritis patients after total knee arthroplasty.

Background

Rheumatoid arthritis (RA) is a systemic autoimmune disease leading to progressive joint destruction and frequently requiring total knee arthroplasty (TKA). However, persistent

postoperative immune activation contributes to disease flares, delayed recovery, and increased complication risk. Precision-based immunomodulation targeting dominant cytokine pathways may improve postoperative outcomes, yet real-world evidence remains limited, particularly in Uzbekistan.

Objectives

To evaluate the effectiveness and safety of a cytokine-guided postoperative therapeutic strategy in patients with RA undergoing TKA.

Methods

This prospective multicenter real-world study included 106 RA patients (ACR/EULAR 2010 criteria) undergoing unilateral TKA across three tertiary centers in Uzbekistan (2024–2025). Patients were stratified based on dominant cytokine profiles (TNF-α, IL-6, IL-1β) measured by ELISA and received pathway-matched biologic therapy (adalimumab, tocilizumab, or anakinra) alongside csDMARDs.

Primary outcome: change in DAS28 at 52 weeks. Secondary outcomes: HAQ-DI, VAS pain, CRP, ESR, cytokine dynamics, remission rates, and safety.

Results

The study included 106 patients with rheumatoid arthritis, of whom 102 (96.2%) completed the 52-week follow-up; the cohort was predominantly female (73.6%) with a mean age of 53.1 ± 9.7 years and high baseline disease activity (DAS28 5.60 ± 0.67; HAQ-DI 2.08 ± 0.41). Patients were stratified into TNF-α–dominant (36.8%), IL-6–dominant (33.0%), and IL-1β–dominant (30.2%) phenotypes. Over 52 weeks, disease activity declined significantly, with DAS28 decreasing to 2.38 ± 0.47 (mean change −3.22; $p<0.001$), while 47% of patients achieved remission and 72% reached low disease activity. Functional outcomes improved in parallel, with HAQ-DI decreasing to 0.87 ± 0.30 and VAS pain reduced by 55 points (both $p<0.001$), accompanied by marked improvements in morning stiffness and knee range of motion. Systemic inflammation

and cytokine levels were substantially reduced, with TNF-α, IL-6, and IL-1β decreasing by 63%, 58%, and 51%, respectively, alongside significant reductions in CRP (−75%) and ESR (−61%) (all $p<0.001$). Phenotype-matched therapy resulted in greater suppression of the dominant cytokine compared with non-matched treatment ($p\leq0.02$) and independently increased the likelihood of remission (OR 1.91; $p=0.014$). Correlation analysis demonstrated significant associations between DAS28 and inflammatory markers, including CRP and cytokines ($p<0.001$). No prosthetic joint infections, implant failures, or deaths were observed, and the overall safety profile was favorable, with only rare serious adverse events and one transient case of neutropenia in the IL-1β group without clinical consequences.

Conclusion

Cytokine-guided postoperative management in RA patients undergoing TKA significantly improves disease activity, functional outcomes, and inflammatory control without increasing complication risk. Personalized, biomarker-driven strategies represent a promising approach for optimizing surgical outcomes in RA.

Keywords

Rheumatoid arthritis; total knee arthroplasty; cytokines; personalized therapy; real-world study

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