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Complications of total knee arthroplasty and the development of late deep infection in patients with rheumatoid arthritis

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ABSTRACT

Aim: This study aimed to assess complications and the presence of late deep infection in patients with rheumatoid arthritis (RA) who underwent primary and revision total knee arthroplasty (TKA).

Material and Method: Between June 1997 and October 2022, cemented TKA that cut the posterior cruciate ligament (PCL) was applied to 50 knees of 34 patients with RA, and posterior-stabilized (PS) revision TKA was applied to 7 knees of 5 patients. All the patients enclosed in this study were adults diagnosed with RA by a rheumatology or physical therapy physician according to the RA diagnostic criteria recommended by the American College of Rheumatology in 1987. The diagnosis of infection was based on the Periprosthetic Infection Diagnostic Criteria of the 2018 International Periprosthetic Joint Infections Consensus Meeting.

Results: Complications were found in 9 (18%) of the 50 knees who underwent primary TKA. Postoperative serous discharge was observed in 3 (6%) knees, serous discharge and late partial rupture of the quadriceps tendon in 1 (2%), early deep infection in 1 (2%), late deep infection in 3 (6%), and hematoma in 1 (2%). Revision surgery was performed on 3 (6%) knees due to infection and on 4 (8%) knees due to aseptic loosening. Complications developed in 2 of these knees who underwent revision TKA, 1 (14.3%) knee with periprosthetic fracture in the femur in the first postoperative year, and 1 (14.3%) knee with early deep infection. Deep vein thrombosis (DVT), pulmonary emboli (PE) and heterotopic ossification (HO) were not observed in any patient.

Conclusion: In patients with rheumatoid arthritis, total knee arthroplasty increased chronic late deep infection and the associated need for revision surgery, and decreased the rates of DVT, PE, HO.

Keywords: Rheumatoid arthritis, total knee arthroplasty, complications

INTRODUCTION

It is stated that more complications are expected in patients with rheumatoid arthritis (RA) who underwent total knee arthroplasty (TKA) compared to patients with osteoarthritis (1,2). It is noted that this situation occurs due to the surgical risk factors stated below.

- 1. Nature of the disease (autoimmune) (1,2),
- 2. Long duration of disease and number of comorbidities (1,2),
- 3. Use of immunosuppressive and nonsteroidal antiinflammatory drugs (NSAIDs) (1,2);
 - Glucocorticoids cause poor bone quality, weakened immune system, and impaired wound healing,
 - Delay in wound healing caused by traditional diseasemodifying anti-rheumatic drugs (DMARD), wound dehiscence, and the risk of opportunistic infection, especially by biological agents,
 - Bleeding side effects of NSAIDs,

- Bone stock insufficiency (periarticular bone osteopenia, osteoporosis, and osteonecrosis),
- 4. Severe joint deformities due to soft tissue involvement and additional difficulties due to other joint involvements (knee, hip, shoulder, ankle) (1-3),
- 5. Cervical spine involvement in 80% of patients and atlantoaxial instability in 30% pose a risk for general anesthesia (Additional medical anesthesia issues) (4),

It is stated that RA is a risk factor for infection (2), and deep wound infections are the most critical complication concerning TKA results in patients with RA (5-8). It has been reported that the preponderance of periodontal disease is increased in patients with RA, and the possibility of enclosing staphylococcus aureus colonization in these patients is higher than in healthy controls (6,7). It has been reported that the need for blood transfusion increases in patients with RA due to anemia, contributing to the risk of infection (9).

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While some similar studies reported that TKA complication rates are higher in patients with RA (8,10), some studies convey that the complication rates are not different (11,12).

It is stated that the nature of the disease and the drugs used affect the duration of the disease, its treatment, surgery, and intricacies (1,2,9,13). Nevertheless, meticulous preparation of the patients for the operation, good timing of the procedure, and proper application (surgical experience) have been ascertained to increase the quality of life and functions in patients with RA (1,5).

This study aimed to assess complications and the presence of late deep infection in patients with RA who underwent primary and revision TKA.

MATERIAL AND METHOD

The study was conducted with the permission of Near East University Scientific Researches Ethics Committee (Date: 29.12. 2022, Decision No: 109-1648). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

This Level III, therapeutic, retrospective study included 50 knees of 34 patients applied with posterior cruciate ligament (PCL)-sacrificing cemented primary TKA, and 7 knees of 5 patients applied with posterior-stabilised (PS) revision TKA between June 1997 and October 2022. All approaches were made with a standard anterior prepatellar incision followed by medial parapatellar arthrotomy. Total synovectomy was performed in all knees maintaining the fatty tissue between the synovium and the anterior femur. The distal femur cut was completed with an intramedullar guide and the proximal tibia cut with an extramedullar guide. Varus/valgus deformities were balanced with medial and lateral release.

At one hour before operation, first-generation cephalosporin (cefazolin sodium) was administered intravenously as prophylaxis at a dosage of 1gr for patients <70 kg and 2 gr for those >70 kg. In all patients, venous thromboembolism (VTE) prophylaxis was provided with low molecular weight heparin (LMWH) starting at 8 hours after operation. The operations were performed under spinal anaesthesia in 27 knee and under spinal-epidural anaesthesia in 23 knee. In all knees, bleeding was controlled and the operation area was washed. All patients were mobilised with full weight-bearing using a walker on the morning of postoperative day 1. After the drain was extracted at postoperative 24 hours, 30 mins of movement, 3-4 times a day, was routinely provided with a continuous passive movement (CPM) device.

All patients enclosed in this study were adults diagnosed with RA by a rheumatology or physical therapy physician by the RA diagnostic criteria recommended by the American College of Rheumatology in 1987 (14).

The drugs utilized by the patients were oral glucocorticoids by 26 (76.5%) and the conventional synthetic disease-modifying anti-rheumatismal drugs (csDMARD) of methotrexate by 10 (29.4%), sulfasalazine by 10 (29.4%), leflunomide by 10 (55.9%), and hydroxychloroquine by 6 (17.6%). Biological DMARDs (bDMARD) and targetted synthetic DMARDs (tsDMARD) were not used by any patient in this study.

A rheumatology or physical therapy specialist managed the anti-rheumatismal drug regimens (stopping preoperatively and/or continuing, and time of re-starting postoperatively). The diagnosis of infection in patients was based on the Periprosthetic Infection Diagnostic Criteria of the 2018 International Periprosthetic Joint Infections Consensus Meeting (15). The patients were followed up postoperatively at 1, 3, 6, and 12 months, and annually thereafter.

Inclusion Criteria

• Based on the criteria of the American rheumatology association, patients who were diagnosed with RA (>18 years old) and used treatment in the Physical Therapy and/or Rheumatology department were included in the study.

Exclusion Criteria

- Secondary inflammatory rheumatic osteoarthritis causes other than RA,
- Metabolic and malignant disease,
- Having a history of patellectomy, fracture around the knee, and infection,
- Patients who underwent high tibial osteotomy and did not respond to the invitation were excluded from the study.

Statistical Analysis

Data acquired in the study were analyzed statistically utilizing SPSS version 23 software. Continuous variables were stated as mean \pm standard deviation (SD) or median (minimum-maximum) values, and categorical values as number (n) and percentage (%). Correlations between drug use and infection were examined using the Chi-square test. A value of p < 0.05 was accepted as the level of statistical significance.

RESULTS

The demographic data of the patients in the study are presented in **Table 1**.

Table 1. Demographic data						
Parameters	Primary total knee arthroplasty		Revision totalknee arthroplasty			
	mean ± SD/n (%)	median (min-max)	mean ± SD/n (%)	median (min-max)		
Age (years)	59.56 ± 11.2	61 (31-80)	60.2 ± 3.5	64 (59-67)		
BMI (Kg/m²)	32.25 ± 4.54	32.4 (20.3-40)	32.7 ± 6.5	30.1 (25.8-39.9)		
Gender						
Female	31 (91.2)		4 (80)			
Male	3 (8.8)		1 (20)			
Total number of patients	34		5			
Total number of knees	50		7			
Side						
Right	10		3 (42.9)			
Left	8		4 (57.1)			
Right/Left in separate sessions	11 (22knees)					
Bilateral in the same session	5 (10knees)					
Follow-up period (months)						
General	132.49 ± 56.38	132.8 (48-304)	83.1 ± 29.1	85.5 (55-126)		
Right	114.87 ± 54.45	116 (48-216)	148 ± 53.3	154 (92-198)		
Left	140.43 ± 66.98	144 (46-304)	45.8 ± 19.2	54.5 (17-57)		
Bilateral	157.67 ± 42.1	161 (114-198)				
Duration of drug use (years)	22.35 ± 8.91	23.5 (7-41)				
SD: standard deviation, BMI: body mass index						

Of the 50 knees on which primary TKA was conducted, revision TKA was performed on 7 (14%). The revision was conducted due to infection in 3 (6%) knees, and due to the use of aseptic loosening in 4 (8%). Complications were found in 9 (18%) of 50 knees who underwent primary TKA. Serous discharge was observed in 3 (6%) knees, serous discharge and late (postoperative 8 years) quadriceps tendon partial rupture in 1 (2%) knee, early deep infection in 1 (2%) knees, and hematoma in 1 (2%) knee (**Table 2**).

Table 2. The complications and revision data of the primary totalknee arthroplasty cases				
	n	%		
Total number of knees	50			
Number of revisions	7	14		
Revision due to infection	3	6		
Right	2	4		
Left	1	2		
Revision due to aseptic loosening	4	8		
Right	1	2		
Left	3	6		
Overall complications	9	18		
Serous discharge, allergy, bullae.	4	8		
Deep infection	4	8		
Early deep infection	1	2		
Late deep infection	3	6		
Quadriceps tendon rupture	1	2		
Hematoma	1	2		

In the knees applied with revision TKA, periprosthetic fracture in the femur developed in 1 (14.3%) knee, and early deep infection in 1 (14.3%) knee (**Table 3**).

 Table 3. The data and complications of the revision total knee

 arthroplasty cases

	n	%		
Revision	7			
Revision due to infection	3	42.9		
Revision due to aseptic loosening	4	57.1		
Revision due to femoral loosening	0	0.0		
Revision due to tibial loosening	7	100.0		
Revision due to loosening in the femur+tibia	0	0.0		
Revision due to patellar loosening	0	0.0		
Overall complications	2	28.6		
Periprosthetic fracture (Femur)	1	14.3		
Deep early infection	1	14.3		
Antibiotic in cement (2 gr Vancomycin) right	2	28.6		
Antibiotic in cement (2 gr Vancomycin) left	0	0.0		
Antibiotic in cement-Gentamicin right	1	14.3		
Antibiotic in cement-Gentamicin left	4	57.1		

There was no significant relationship between infection and drugs used (p=0.156) (**Table 4**). The rate of infection was determined to be 10% in methotrexate users, 30% in insulfasalazine users, 21.1% in leflunomide users, 33.3% in hydrocychloroquine users, and 11.5% in those using oral glucocorticoids.

*	een the drugs used and infection		
	Absent	Present	P*
Methotrexate	9 (90)	1 (10)	
Sulfasalazine	7 (70)	3 (30)	
Leflunomide	15 (78.9)	4 (21.1)	0.156
Hydroxychloroquine	4 (66.7)	2 (33.3)	
Oral glucocorticoids	23 (88.5)	3 (11.5)	
*Chi-square test			

DISCUSSION

Following TKA, major complications (deep surgical site infection, wound opening, pulmonary embolism, fracture, reoperation) have been reported at rates between 5.55% and 14.4%, and minor complications (superficial surgical site infection, deep vein thrombosis, bleeding, peripheral nerve injury) at 2.86%-46.6% (16,17). Previous some studies reported that TKA complication rates are higher in patients with RA compared to OA cases (10), while some studies have reported no significant difference. (11). In the current study, complications were found in a total of 9 (18%) knees of primary TKA cases, including major complications (deep infection) in 4 (8%) knees, and minor complications in 5 (10%) (serous discharge, hematoma, quadriceps tendon partial rupture). The rate of complication in the primary TKA cases was found to be at a similar level to OA cases within the limits noted in literature. Following revision TKA in RA patients, the rate of complication has been reported to be 19-28% (18). In the current study, only major complications (deep infection and periprosthetic femur fracture) developed in 2 (28.6%) knees applied with revision TKA.

Following primary TKA, the rates of overall infection have been reported to be 1-2%, superficial infection 10%, and deep infection 0.3-3.9% (12,19,20), whereas in revision cases, the rate of overall infection has been stated to be 0-10% (21-23). For patients with RA, the general infection rate has been reported to be 1.4-4.2% (12,19,20), increasing to 5.9% in revision (21-23). In previous studies, infection rates following primary TKA have been seen to be 2-3-fold greater in patients with RA compared to patients with OA (6-8). However some studies have reported similar rates (12). Lee et al. (22) reported that a significantly higher rates of deep surgical site infection in patients with RA after TKA compared to patients with OA, but the superficial infection rates were similar. Rodriguez et al. (20) found that a delayed infection (mean 7 years) in 4.1% of patients with RA applied with primary TKA. In a study by Mortavazi et al. (21), the infection rate in revision patients was reported to be 19%. In the current study of primary TKA cases, findings of superficial infection, such as postoperative serous discharge, allergy and bullae, were determined in 4 (8%) knees and recovery was obtained in all of these with medical treatment. In 1 (2%) knee determined with early deep infection at one month postoperatively, treatment was applied with debridement, antibiotherapy, insert change and implant preservation. Late (delayed) deep infection was determined in 3 (6%) knees, at 4, 5, and 6 years respectively, and all were treated with single-stage revision. Early deep infection developed in one (14.2%) of the knees applied with revision. Recovery was obtained with treatment of debridement, antibiotherapy, insert change and implant preservation. The rate of superficial infection in the current study was similar to OA cases, and the rate of deep infection was determined to be higher than OA cases.

Corticosteroids suppress the inflammatory phase of wound healing and change the re-shaping of the wound, but it has been stated that the doses used in RA are not of a high enough level to create these problems (1,3,6). Methotrexate reduces the stretching power of the wound, but the doses given in RA have been reported to not generally affect this and therefore healing is not affected (24). The use of tumour necrosis factor alpha (TNF-a) inhibitors has been reported to create more wound separation and infection (6,7). Previous studies have stated that doses of corticosteroids should be altered preoperatively and continued during the operation if necessary; methotrexate should not be stopped but used continuously, and this aids in healing and does not increase the risk of infection, and biological agents should be stopped preoperatively due to increased infection rates (1,3). The current study found no significant relationship between infection and the use of corticosteroids, methotrexate, sulfasalazine, leflunomide, or hydroxychloroquine.

The incidence of periprosthetic fracture (PPF) after TKA has been reported to be 0.3-5.5%. Previous studies have shown that PPF after TKA usually tends to occur in the femur supracondylar region 2 years after the operation, and the reason is usually anterior femoral notching (25,26). It has been stated that in 35.3% of revisons, PPF occurs within two years, and the reason for failure is associated with aseptic loosening (27). The risk of PPF in patients with RA has been shown to increase due to the nature of disease, and poor bone quality associated with chronic use of steroids and DMARDs (1,28). A study by Choi et al. (1) in RA who underwent TKA reported that a significant increase in supracondylar PPF incidence after mean 11.9 years (range, 9-14 years). Lee et al. (29) indicated that patients with RA were at risk of PPF occurring after mean 11.4 years postoperatively. PPF was not detected in any of the primary TKA cases in the current study. This was thought to be due to the support provided for the patients in respect of osteoporosis, that care was taken during the operation not to create notches in the femur, and that the mean age of the patients was 59.6±11.2 years. However, PPF developed following a fall at 1 year postoperatively in one patient who underwent revision TKA, and this was treated with open reduction and internal fixation with a locking plate.

In TKA patients not administered with thromboprophylaxis, deep vein thrombosis (DVT) has been reported at rates of 50-70%, pulmonary thromboemboli (PTE) at 5%, and fetal PTE at 1-4%. In patients who have been administered thromboprophylaxis, these rates have been reported to

be DVT 0.9-5%, PTE 0.27-1.1%, and fetal PTE 0.1-0.5% (30). In patients with RA who have undergone TKA, RA has been noted to be protective against VTE (8), and the VTE incidence is 3-10-fold lower than OA patients, which has been attributed to the patients being younger and the use of NSAIDs (31). However, in some studies reported that no difference in terms of VTE (32), while there are some studies t reported that RA to be a risk factor for VTE (13). Besides, it has been reported that the incidence of VTE is 2.4% higher in patients with RA than OA patients (33). In a study of RA patients applied with TKA, the risk of VTE was lower, but in patients treated with biological DMARDs the VTE incidence was determined to be 5-fold higher compared to RA patients not treated with biological DMARDs (6). In the current study, none of the patients were treated with biological DMARDs or targetted synthetic DMARDs. Pulmonary embolism or DVT were not determined in any of the current study patients. This was considered because VTE prophylaxis was administered with LMWH starting from 8 hours postoperatively, followed by oral anticoagulants for 14 and/or 35 days, and antithrombocyte activity occurred because of the long-term use of NSAIDs in RA.

Quadriceps tendon rupture following TKA is uncommon, and has been reported to be observed at rates between 0.1% and 1.1% (34,35). In the current study, late (postoperative 8 years) quadriceps tendon partial rupture was seen in 1 (2%) knee due to a fall. As the patient had no evident loss of extension, treatment was nonoperative. Dobbs et al. (34) reported satisfactory results and fewer complications with non-operative treatment of quadriceps tendon partial rupture.

The formation hematoma around the knee after TKA is frequently observed and can cause patients discomfort and concern about the operation's success. This condition has been reported to be associated with intraoperative tourniquet use, postoperative drainage methods, VTE prophylaxis, and male gender. However, the underlying specific mechanisms generally remain uncertain (36). In addition to the conditions present in patients with RA, long-term use of NSAIDs can increase the risk of bleeding. Hematoma developed in 1 (2%) knee of one male patient in the current study and this was successfully treated with removal of the sutures, drainage and dressings.

Heterotopic ossification was not determined in any patient in the current study. This was thought to be due to the use of corticosteroids and NSAIDs, which were continued postoperatively. In TKA cases, the rate of heterotopic ossification has been reported as 0-42% (37). It has been reported that this rate is lower in RA patients and this may be due to the use of NSAIDs and corticosteroids (38). No neurovascular injury, instability, or dislocation was reported in any of the current study patients.

Limitations

The main limitations of this study are its retrospective design, relatively low sample size, and lack of an OA control group for comparison.

CONCLUSION

RA is a chronic, systemic, autoimmune disease, and because of comorbidities a relative increase is observed in chronic late deep infection and associated revision, and a decreased in DVT, pulmonary embolism and heterotopic ossification due to the long-term use of NSAIDs and glucocorticosteroids. There was no significant relationship between the drugs (oral glucocorticoids and DMARDs) used by our patients and the infection. We did not detect an increase in PPF rates.

In patients with RA who undergo TKA, although complication rates have been reported to be higher than in OA cases, TKA can be performed safely and complications can be reduced with the following steps;

- 1. A multidisciplinary approach,
- 2. Adjustment of the time of stopping and re-starting drugs by establishing good direct communication with the rheumatologist (to provide a balance between reducing the risk of infection and suppression of disease activity),
- 3. Preparing the patient for the operation in respect of comorbidities,
- 4. Correct timing of the operation,
- 5. Preoperative prophylaxis,
- 6. An experienced surgeon,
- 7. Correct surgery under sterile conditions.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of Near East University Scientific Researches Ethics Committee (Date: 29.12.2022, Decision No: 109-1648).

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

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