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Functional and biochemical improvement following total knee arthroplasty in early postoperative period

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SUMMARY

OBJECTIVE: There are very few studies about total knee arthroplasty biomechanical and biochemical effects in the early postoperative period. The aim of this study was to investigate the effect of total knee arthroplasty on pain intensity, knee joint valgus angle, malalignment, functional status, knee joint position sense, and cytokine levels.

METHODS: A total of 29 patients (female/male: 24/5) who underwent total knee arthroplasty were included in the late-stage knee osteoarthritis group, and 22 patients (female/male: 13/9) with grade 4 osteoarthritis were included in the early-stage knee osteoarthritis group. The visual analog scale and the Western Ontario and McMaster Universities Osteoarthritis Index were used to evaluate the pain intensity and functional status. Alignment and knee position sense measurements were also calculated. Systemic venous blood samples were taken to evaluate the interleukin-6, tumor necrosis factor-alpha, and interleukin-1 beta cytokine levels.

RESULTS: In the study group, there were positive improvements in pain intensity, functional status, valgus angle, malalignment, amount of joint position sense deviation at 70° knee flexion angle parameters, and interleukin-6 of patients at the postoperative 6th week compared to the preoperative period ($p<0.05$). The patients in the study group had similar or better results in pain intensity, functional status, valgus angle, malalignment, amount of joint position sense deviation at 35°, 55°, and 70° knee flexion angles parameters, and in interleukin-6, compared to the control group at postoperative 6th week.

CONCLUSION: Total knee arthroplasty provides improvements in pain, function, valgus angle, joint position sense, and interleukin-6 in the early postoperative period.

KEYWORDS: Knee arthroplasty. Interleukins. Proprioception. Radiography. Osteoarthritis.

INTRODUCTION

Osteoarthritis (OA) is one of the most common chronic peripheral joint diseases. Loss of function and pain are important symptoms, and one of the main goals of treatment is to improve the quality of life[1]. Total knee arthroplasty (TKA) is a favorite surgical approach aimed at improving joint function and relieving pain intensity. In the United States, the incidence rate of TKA is expected to increase[2], thus increasing the financial burden. Biomechanical and biochemical changes associated with TKA are being studied but not clearly explained. So, it is important to show the changes in pain intensity, lower extremity alignment, functional status, joint position sense (JPS), and cytokine levels (IL-6, TNF-α, and IL-1β) of patients who underwent TKA.

Related literature generally focused on biomechanical gains such as reducing pain and increasing functional status after TKA. However, there is very limited evidence about cytokines, and JPS in the acute phase after TKA. So, this situation requires examining cytokines (IL-6, TNF-α, and IL-1β) after TKA. The investigation of cytokine levels in terms of response to degenerative processes and surgical stress in the joint can be guided. Biomechanical deteriorations in the knee joint affect patients' knee JPS adversely[3]. Although many studies show evidence that TKA improves proprioception in suitable surgical candidates, the overall effect of TKA on proprioception is controversial[4]. More studies are still needed on this subject in a holistic approach.

The main hypothesis of the study is to investigate whether there is a functional and biochemical effect of TKA surgery. Another hypothesis is to investigate whether the functional parameters and inflammatory cytokines in the group undergoing

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TKA reach levels similar to those in the OA group 6 weeks after the operation without any indication for surgery. So, the purpose of this study was to indicate the early effects of TKA on pain intensity, knee joint valgus angle, malalignment, functional status, knee JPS, and cytokine levels in patients with late-stage knee osteoarthritis (LSKO), and to compare the early-stage knee osteoarthritis (ESKO) and LSKO in terms of these parameters.

METHODS

This study was designed as a prospective cohort study. It was completed with 51 OA patients (female/male: 37/14): 29 in the LSKO group (female/male: 24/5) and 22 in the ESKO group (female/male: 13/9). They were evaluated with complaints of knee pain by the Department of Orthopaedics and Traumatology, Farabi Hospital, Faculty of Medicine, Karadeniz Technical University. The OA severity level was determined according to the Kellgren-Lawrence classification system. Patients with grade 4 degeneration levels who had surgical indications between the ages of 45 and 75 years were included in the LSKO group (n=29), and they underwent surgery. Patients without surgical indication with lower than 3 OA severity were included in the ESKO group (n=22), and they did not undergo surgery. Patients with surgical history of the ipsilateral side, neuropathic pain, loss of sensation, and systemic, chronic, and infectious diseases were excluded from the study. First, 41 cases were evaluated for the LSKO group in the preoperative period; 11 patients who did not come for follow-up after discharge and 1 patient who was hepatitis C virus positive were excluded.

This study was approved by the Karadeniz Technical University Scientific Research Ethics Committee (May 25, 2018; no. 2018/91). Patients were informed about the study. They read and signed the written informed consent form.

After the sociodemographic features were recorded, pain intensity, valgus angle and malalignment, functional status, JPS, and cytokine levels (IL-6, TNF-α, and IL-1β) were evaluated. Measurements were taken once from the ESKO group, and twice from the LSKO group in preoperative and postoperative 6th weeks.

Main outcome measures

Pain intensity: The pain intensity was evaluated by the visual analog scale. The patients marked their intensity of pain on rest and walking on a vertical line of 10 cm (0: no pain, 10: unbearable pain)[5].

Valgus angle and malalignment assessment: They were calculated on the knee anteroposterior direct x-ray image by an experienced orthopedist. The valgus angle was calculated as the angle facing the lateral between the anatomical axis of the tibia and the anatomical axis of the femur. For malalignment measurement, vertical lines were drawn from the edges to the proximal joint face of the tibia and the distal joint face of the femur. The distance between these perpendicular lines was recorded[6].

Functional status: The Western Ontario and McMaster Universities Arthritis Index (WOMAC) was used. The validity and reliability of the index in Turkish were determined by Tüzün et al.[7] This 24-item index has three subdimensions: pain, stiffness, and physical function. A high score means a low level of functional status[7].

JPS: In our study, the protocol developed by Hurley[8] was used. The knee was passively brought to 70° at a rate of 10°/s starting from 90° of flexion. After holding it for 3 s at this angle, it was passively brought to its initial position at the same speed. Then, the patient was instructed to actively bring the knee to the targeted angle and hold this position for 5 s. The amount of deviation from the target angle was recorded. The average of their trials was calculated for the final score. The same evaluations were performed for 55° and 35° knee flexion angles, respectively.

Cytokine level: Systemic venous blood samples were taken. IL-6, TNF-α, and IL-1β cytokine levels were examined. Venous blood samples were taken to separator gel biochemistry tubes and allowed to clot for 30 min at room temperature. The clotted blood samples were centrifuged for 10 min at 3000 rpm. Serum samples obtained as a result of centrifugation were divided into tubes with micro-volume caps and stored at -80°C. All the samples in the LSKO and ESKO groups were analyzed simultaneously using kits that can measure using the enzyme-linked immunosorbent assay method.

Statistical analysis

The SPSS 21.0 (Statistical Package for Social Science, Chicago, IL, USA) package program was used for the analysis. Student's t-test and Mann-Whitney U test were used in the preoperative and postoperative comparisons of the groups. Paired-sample t-test and Wilcoxon test were used to compare the measurements. Mean, standard deviation, and total number were calculated. The significance level was taken as $p<0.05$. The G*Power 3.1.9.2 program was used for sample size. When the effect size was accepted as 0.5 with 5% type 1 error and 80% power according to repeated measures differences analyses, it was calculated as 28 patients for LSKO. The current power was calculated as 82% for the results.

RESULTS

Sociodemographic features and preoperative outcome measurements were shown in Table 1.

Pain intensity, functional status, valgus angle, malalignment, and JPS deviation in 70^0 and IL-6 showed significant improvement in the postoperative 6th week compared to the preoperative period in the TKA group ($p<0.05$). There was no significant difference among TNF-α, IL-1β, and JPS deviation in 35° and 55° in preoperative and postoperative periods ($p>0.05$) (as can be seen in Table 2).

According to the results of the relationship between the LSKO and ESKO groups 6 weeks after TKA, TNF-α and IL-1β values were significantly higher, while pain intensity during walking and malalignment amount data were lower in the LSKO group ($p<0.05$). There was no significant difference in pain intensity during rest, WOMAC score, valgus

Table 1. Sociodemographic and preoperative outcome measurements.

Parameters		LSKO group X±SD	ESKO group X±SD	p-value
Age (years)		67.55±6.55	54.18±8.25	<0.001*
Body weight (kg)		82.31±8.64	82.95±13.73	0.84
Body height (cm)		161.34±6.69	166.18±10.60	0.07
Body mass index (kg/m²)		31.72±3.79	30.25±5.59	0.27
Pain intensity	During rest	4.04±2.87	2.10±1.78	0.004*
	During walking	6.88±2.09	4.46±2.77	0.001*
Valgus angle		184.23±7.31	177.56±2.80	<0.001*
Malalignment		5.46±2.67	2.75±1.96	<0.001*
WOMAC score		72.72±13.13	33.64±12.44	<0.001*
Amount of joint position sense deviation	35^0	6.11±6.06	8.27±7.39	0.25
	55^0	6.08±4.04	5.43±3.64	0.56
	70^0	10.40±9.21	5.89±4.89	0.04*
Cytokine	IL-6	203.90±73.76	139.04±90.68	0.007*
	TNF-α	54.54±3.82	34.18±14.65	<0.001*
	IL-1β	113.14±11.17	86.60±21.42	<0.001*

LSKO: late-stage knee osteoarthritis; ESKO: early-stage knee osteoarthritis; IL-6: interleukin 6; TNF-α: tumor necrosis factor-alpha; IL-1β: interleukin-1 beta; WOMAC: Western Ontario and McMaster Universities Osteoarthritis Index; X: mean; SD: standard deviation. *Statistically significant differences ($p<0.05$).

Table 2. Differences between preoperative and 6 weeks after TKA for LSKO group.

Parameters		Preoperative	Postoperative 6th week	p-value
Pain intensity	During rest	4.07±2.87	1.26±1.35	<0.001*
	During walking	6.88±2.09	2.10±1.69	<0.001*
Valgus angle		184.23±7.31	176.26±2.91	<0.001*
Malalignment		5.46±2.67	1.84±2.66	<0.001*
WOMAC score		72.72±13.13	27.92±14.24	<0.001*
Amount of joint position sense deviation	35^0	6.11±6.06	6.42±5.89	0.85
	55^0	6.08±4.04	5.26±4.91	0.26
	70^0	10.40±9.21	6.02±4.96	0.02*
Cytokine	IL-6	203.90±73.76	161.04±30.71	0.002*
	TNF-α	54.54±3.82	52.18±4.65	0.09
	IL-1β	113.14±11.70	114.45±14.43	0.83

LSKO: late-stage knee osteoarthritis; ESKO: early-stage knee osteoarthritis; IL-6: interleukin 6; TNF-α: tumor necrosis factor-alpha; IL-1β: interleukin-1 beta; WOMAC: Western Ontario and McMaster Universities Osteoarthritis Index; X: mean; SD: standard deviation. *Statistically significant differences ($p<0.05$).

Table 3. Comparison of the variables between the LSKO group postoperative 6th week results and the ESKO group results.

Parameters		LSKO group X±SD	ESKO group X±SD	p-value
Pain intensity	During rest	1.26±1.35	2.10±1.78	0.06
	During walking	2.10±1.69	4.46±2.77	0.001*
Valgus angle		176.26±2.91	177.56±2.80	0.14
Malalignment		1.84±2.66	2.75±1.96	0.01*
WOMAC score		27.92±14.24	33.64±12.44	0.14
Amount of joint position sense deviation	35^0	6.42±5.89	8.27±7.39	0.34
	55^0	5.26±4.91	5.43±3.64	0.89
	70^0	6.02±4.96	5.89±4.89	0.92
Cytokine	IL-6	161.04±30.72	139.04±90.68	0.28
	TNF-α	52.18±4.65	34.18±14.66	<0.001*
	IL-1β	114.46±14.43	86.60±21.42	<0.001*

LSKO: late-stage knee osteoarthritis; ESKO: early-stage knee osteoarthritis; IL-6: interleukin 6; TNF-α: tumor necrosis factor-alpha; IL-1β: interleukin-1 beta; WOMAC: Western Ontario and McMaster Universities Osteoarthritis Index; X: mean; SD: standard deviation. *Statistically significant differences (p<0.05).

angle, and JPS deviation in 35°, 55°, and 70° (p>0.05) (as can be seen in Table 3).

DISCUSSION

In this study, patients who underwent TKA recovered compared to those who underwent pre-surgery in terms of pain intensity, valgus angle, malalignment, functional status, JPS deviation in 70°, and IL-6. They had pain intensity level during rest, valgus angle, functional status, JPS, and IL-6 similar to the ESKO group.

Pain intensity after the TKA is affected by many physical, radiological, and biochemical factors[9]. Patients in the LSKO group had higher preoperative pain intensity than patients in the ESKO group. This may result from higher degenerative conditions in the knee in the surgery group[10]. In our study, it was seen that high pain intensity tends to decrease over time in the postoperative period, and the pain intensity at rest in the postoperative 6th week was lower than the individuals in the ESKO group. Similarly, Si et al.[11] reported that pain intensity during rest increased on the first postoperative day compared to the preoperative period and decreased in the following days. Pain intensity during activity decreased after the surgery, but it did not decrease to the level at rest. This may be a natural result of patients' efforts to exercise, and emotional conditions such as fear of movement and anxiety. More studies are still needed on this subject.

In our study, similar to the literature, increased valgus angles were corrected by surgery and brought to a similar level with individuals in the ESKO group[12]. In addition, the malalignment was improved to a better level than the ESKO group in the postoperative 6th week.

In our study, functional status in the postoperative 6th week of the LSKO group was improved. They had a similarity to ESKO. After surgery, especially the decrease in pain intensity contributed to the improvement in walking and functional status of the patients[13]. In another study, it was reported that the use of anti-inflammatory drugs may cause a decrease in WOMAC knee scores[14].

It was observed that the patients in the LSKO and ESKO groups have similar knee JPS deviation at postoperative 6th week. In LSKO, more deviation in 70° in preoperative may be due to increased stress in the joint at an advanced knee flexion degree and hence the increased pain. After TKA, these deviations became similar to those in ESKO. The knee joint is very important for proprioception due to the mechanoreceptors it contains. So, in early postoperative period, follow-up could improve functional mobility. Lowering the valgus angle to normal can have positive effects on knee proprioception. However, for these patients, loss of knee proprioception may continue for a year[15]. Long-term studies are still needed.

In the LSKO group, IL-6 decreased to a level similar to that of ESKO at the postoperative 6th week. TNF-α and IL-1β values decreased but were not similar to the level of ESKO. The IL-6 value is the most important cytokine parameter affected by surgery in our study. Indeed, serum IL-6 level is one of the best reflecting indicators of surgical stress and is the laboratory indicator with the greatest diagnostic accuracy for periprosthetic infection.[16-18] In related literature, serum IL-6 levels of individuals who have undergone

TKA show a significant increase in early postoperative days and are almost equal to the preoperative period in the 6th week[18-21]. Cytokine levels can be evaluated as a local inflammatory response or a systemic inflammatory response[22]. In our study, serum cytokine levels were evaluated. According to the literature, the contralateral side knees of individuals who have undergone TKA mostly have moderate or severe OA[23]. Therefore, the positive effects of surgery on current cytokine levels can be limited depending on the other side. More studies are still needed.

The emotional state could be effective in reducing pain and cytokine levels. The emotional states of the patients were not evaluated, which is the limitation of the study. Furthermore, there are some clinical implications. First, TKA provides biomechanical and biochemical improvements. Second, valgity angle and malalignment decrease after TKA. Third, the IL-6 value is one of the most important cytokine parameters affected by surgery. These findings will provide information to physicians, physiotherapists, and health professionals working in this field on medication and rehabilitation approaches in pre- and post-surgical pain control.

CONCLUSION

The TKA provides improvements in pain, function, valgus angle, JPS, and IL-6 in the early postoperative period. In the postoperative 6th week, patients who had TKA had similar clinical and functional results in terms of IL-6 level, pain intensity at rest and walking, WOMAC score, valgus angle, malalignment amount, and knee JPS to patients in the early stage of knee OA. These findings are also very important in determining the treatment approaches and patients' expectations on knee osteoarthritis.

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AUTHORS' CONTRIBUTIONS

AE, ME, OA: Conceptualization, Data curation, Formal Analysis, Writing – original draft, Writing – review & editing. **KC, SÖY, İP, SCK:** Conceptualization, Data curation, Formal Analysis.

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