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Original Article

Ultrasonographic Evaluation of the Distal Femoral Cartilage Thickness in Parkinson's Patients

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Abstract

Objectives: Both Parkinson's disease (PD) and osteoarthritis (OA) are characterized by chronic inflammation and tissue degeneration. The aim of this study is to investigate the relationship between PD and distal femoral cartilage thickness (DFCT). Our study is the first in the literature to measure DFCT in PD. **Methods**: 68 patients with PD and 30 healthy individuals participated. The patient group was divided into three subgroups, according to the Hoehn Yahr stages (HYS): mild, moderate and severe. Patient subgroups and the control group were compared with each other in terms of neutrophil-lymphocyte ratio (NLR), C-reactive protein (CRP), and DFCT. **Results**: The NLR and CRP levels of the PD patients were higher than the values of the healthy people. The DFCT values of the mild PD subgroup were significantly higher than those of the control group, except for one value. The DFCT values of the moderate PD subgroup and the healthy group were similar. The DFCT values of the severe PD subgroup were lower than the values of the healthy group. **Conclusions**: Our study showed the presence of ultrasonographic evidence consistent with early signs of cartilage destruction in early-stage PD disease. As the PD stage progressed, the cartilage thickness decreased accordingly.

Keywords: Distal Femoral Cartilage Thickness, Inflammation, Osteoarthritis, Parkinson's Disease, Ultrasound

Introduction

PD is a neurodegenerative disorder with progressive signs and symptoms such as bradykinesia, rigidity, resting tremor, apathy and postural instability (balance and gait disturbance) due to the destruction of dopaminergic neurons[1,2]. Aggregation of α-synuclein proteins known as Lewy bodies are seen in the central and peripheral nervous system[3]. Pathological changes associated with PD begin 10 years before symptoms appear. The mechanisms underlying PD are still not fully understood. While 5-10% of PD is genetic and early onset, the remaining cases are idiopathic, and aging is understood to be the cause. In addition to genetic factors, environmental factors that stimulate inflammation such as bacterial and viral infections, pesticides, toxins and heavy metals also contribute to the emergence of the disease[4]. In recent years, accumulating evidence has shown that OA, in which low-level chronic inflammation is observed, also exacerbates PD[1,5-7]. However, all these studies were retrospective and none of them evaluated cartilage thickness in patients with PD and the OA development in PD disease. This study aims to determine distal femoral cartilage thicknesses by ultrasonographic evaluation of both knees in individuals with idiopathic PD and in the control group and to compare these values between the groups. Thus, it was also aimed to examine whether there is a predisposition to knee OA in PD patients and evaluate the relationship between blood inflammatory parameters, balance and motor function and cartilage thickness in the patient group. Our study is the first in the literature to measure DFCT in PD.

The authors have no conflict of interest.

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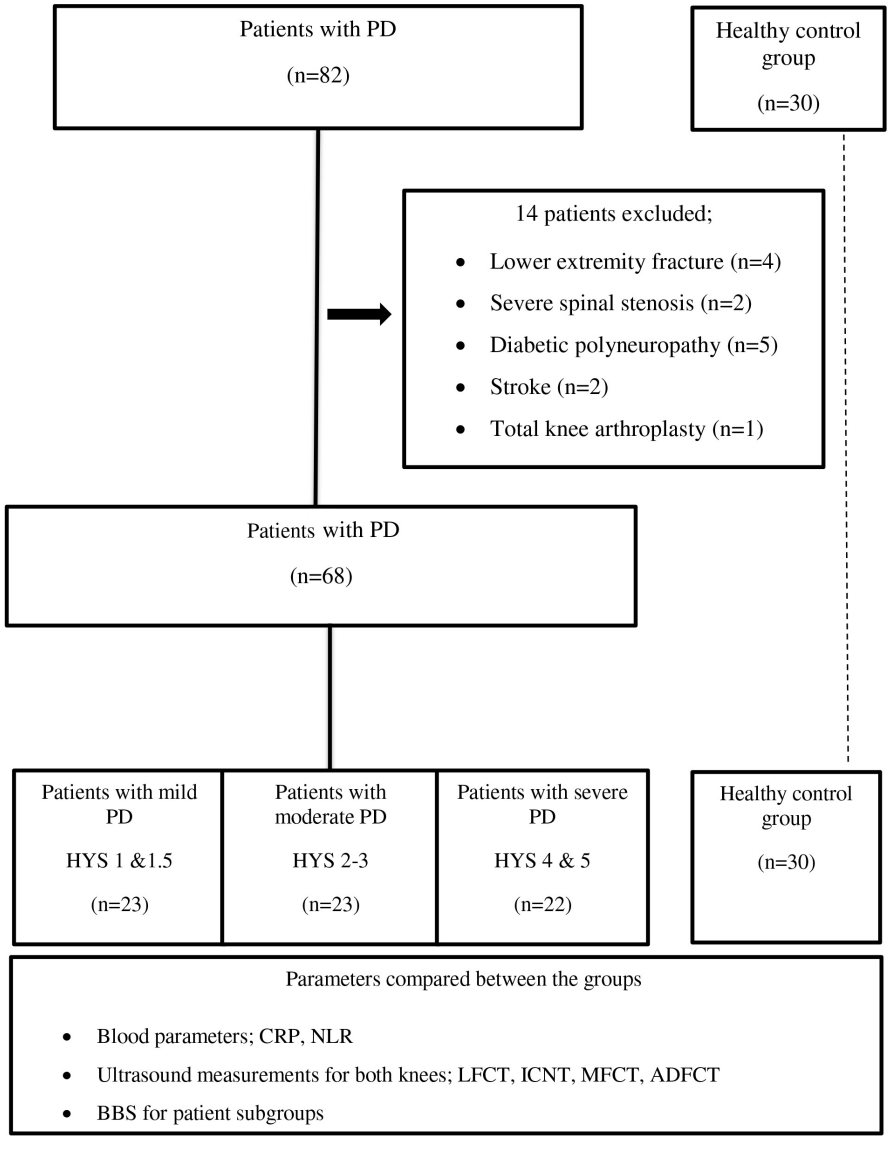

Figure 1. Flow chart.

Materials and Methods

Study Design and Participants

Our study included 68 patients who applied to our outpatient clinics and were diagnosed with idiopathic PD according to the UK Parkinson's Disease Association Brain Bank Diagnostic Criteria, and 30 healthy individuals as a control group. The healthy control group consisted of healthy relatives of the patients (their wives or husbands) and healthy individuals who applied for bone densitometry measurement and whose results were within the normal range. Some of the patients who applied for reasons that did not affect the legs, such as acute cervical muscle pain or acute shoulder pain, were also included in the control group. The control group consisted of healthy individuals with similar characteristics to the patient group in terms of age, gender distribution, weight, height and BMI. Exclusion criteria were rheumatologic disease, malignancy, fracture in the lower extremity, other neurological disease and total knee arthroplasty (Figure 1). This study was carried out between November 2021 and August 2022.

Demographic Features, Laboratory and Clinical Examination Tests and Subgroups

Gender, age, body mass index and duration of PD of the patients were noted. The balance level of the patients was evaluated with Berg Balance Scale (BBS), and motor function

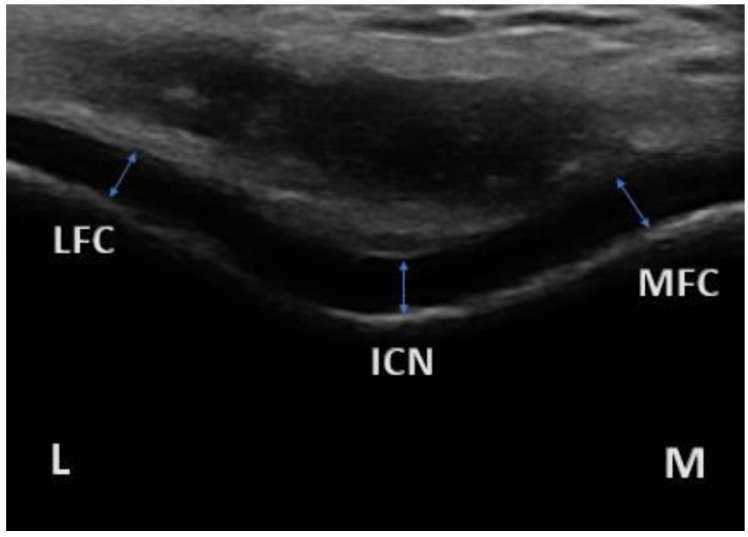

Figure 2. Measurement of the distal femoral cartilage thicknesses from three different points. LFC, lateral femoral condyle; ICN, intercondylar notch; MFC, medial femoral condyle; L, lateral; M, medial.

level was evaluated with a modified Hoehn-Yahr (HY) Scale. Similar to the PD classification made by Vitório et al., we considered HYS 1 and 1.5 as mild disease and HYS 2-3 as moderate disease in our study[8]. We considered the remaining stages 4 and 5 as severe disease. A BBS score below 20 was considered as bad, and above 40 was considered as good. The score between the range of 20 and 40 was accepted as moderate balance[9].

Hemogram parameters and CRP levels were studied in the patient and control groups via ABX Pentra 120 (Horiba) and Cobas 8000 (Roche), respectively. The NLR was calculated by dividing the neutrophil count by the lymphocyte count using the hemogram parameters.

Ultrasonographic Measurements

The DFCT measurements of the patient group and the healthy control group were performed with an US machine, Toshiba Aplio 500, with a linear probe in the transverse position from the suprapatellar region while the subjects were lying supine and their knees were maximally flexed. Cartilage thicknesses were measured from the mid-points of the medial femoral condyle, inter-condylar area, and lateral femoral condyle. Cartilage thickness was determined by measuring the distance between the thin hyper-echoic line at the joint gap-cartilage interface and the sharp hyper-echoic line at the cartilage-bone interface (Figure 2), similar to the work of Abraham et al. The reliability and validity of the ultrasound in OA diagnosis was shown by Abraham et al.[10]. Each measurement was made three times and average values were taken. The average cartilage thickness of the right and left knee was calculated by summing the measurements made from these three different points for both knees and then dividing the sum value into three. All ultrasonographic measurements were made by a physiatrist with 7 years of experience.

Statistical Analysis

Descriptive statistics were shown as frequency and percentage for categorical data, and arithmetic mean ± standard deviation for continuous data. Whether the continuous data were normally distributed or not was evaluated with the Shapiro-Wilk Test and coefficient of variation. Pearson Chi-Square Test was used to evaluate the statistical difference between categorical variables in the PD and control groups. If the continuous variables were normally distributed, the Independent-samples t-test was used to evaluate the statistical difference between the two groups; If not normally distributed, the Mann Whitney-U Test was used. In terms of continuous variables, the statistical difference between the four groups was determined by the One-Way Anova test if there was an assumption of normal distribution. If not normally distributed, the Kruskal Wallis Test was used. If a significant difference was found between the groups with One Way Anova, the Tukey Post-hoc Test was used for pairwise comparisons. If a significant difference between the groups was found with the Kruskal Wallis Test, the Bonferroni corrected and double Mann Whitney-U Tests were used for post-hoc analysis. Spearman correlation analysis was performed for the relationship analysis between the variables. All analyzes were performed with the SPSS 22.0 statistical package program and $p<0.05$ was considered statistically significant in all statistical analyses. In cases

Table 1. Findings of Parkinson's and control groups.

		Patient Group (n=68)	Control Group (n=30)	*p*
Age (years)		67.72 ± 7.59	66.16 ± 6.16	0.327**
Gender	Female (%)	27 (39.7)	12 (40.0)	0.978*
	Male (%)	41 (60.3)	18 (60.0)	
Weight (kg)		77.77 ± 10.87	80.03 ± 10.11	0.337**
Height (m)		1.65 ± 0.08	1.66 ± 0.07	0.687**
BMI (kg/m²)		28.46 ± 4.44	28.71 ± 4.43	0.801**
CRP levels		4.87 ± 2.29	2.49 ± 0.96	**< 0.001****
NLR		2.68 ± 0.76	1.95 ± 0.71	**< 0.001****
RLFCT (mm)		1.89 ± 0.42	2.04 ± 0.26	0.069**
RICNT (mm)		1.99 ± 0.46	1.99 ± 0.20	0.998**
RMFCT (mm)		1.99 ± 0.46	2.02 ± 0.26	0.801**
RADFCT (mm)		1.96 ± 0.41	2.02 ± 0.21	0.463**
LLFCT (mm)		1.90 ± 0.40	1.98 ± 0.17	0.303**
LICNT (mm)		2.00 ± 0.51	2.04 ± 0.18	0.753**
LMFCT (mm)		1.94 ± 0.38	1.99 ± 0.19	0.471**
LADFCT (mm)		1.95 ± 0.40	2.00 ± 0.18	0.486**
R-LADFCT (mm)		1.95 ± 0.40	2.01 ± 0.19	0.461**

BMI, body mass index; CRP, C-reactive protein; NLR, neutrophil lymphocyte ratio; RLFCT, right lateral femoral condyle thickness; RICNT, right intercondylar notch thickness; RMFCT, right medial femoral condyle thickness; LLFCT, left lateral femoral condyle thickness; LICNT, left intercondylar notch thickness; LMFCT, left medial femoral condyle thickness; RADFCT, right average distal femoral condyle thickness; LADFCT, left average distal femoral condyle thickness; R-LADFCT, right-left average distal femoral condyle thickness.

where numerical variables were normally distributed, the ANOVA test was used to compare the differences between independent groups. If there are at least 22 people in each of the four groups, the power of the study was calculated to be 81% with a margin of error of 5% and an effect size of 0.365.

Results

Sex, age, weight, height, BMI and ultrasonographic cartilage measurements of the right and left knees were similar between the patient and healthy control groups (p>0.05). The mean CRP and NLR levels were found to be significantly higher in the Parkinson's group (p values<0.001). All cartilage thickness values were similar between the PD and healthy control groups (all p values >0.05) (Table 1).

Gender distribution and mean height values were similar between the mild PD subgroup, moderate PD subgroup, severe PD subgroup, and healthy control group (all p>0,05). There was a significant difference between the groups in terms of mean values of age, weight, and BMI (p<0.001, p<0.001, p<0.001, respectively). Age was higher, and weight and BMI were lower in the severe PD subgroup than in the mild and moderate PD subgroups and healthy control group (Table 2). There was a significant difference between all the PD subgroups in terms of disease duration (p < 0.001); the highest was found in the severe PD subgroup and the lowest in the mild PD group. There was a significant difference between all PD subgroups in terms of mean values of HYS and BBS score (all p≤0.001). The lowest mean BBS score was in the severe PD subgroup and the highest in the mild PD subgroup. The mean CRP levels of all three PD subgroups were higher than the values of the healthy control group (all p≤0.001). The mean NLR levels of all three (mild, moderate and severe) PD subgroups were higher than the values of the healthy control group (p values 0.017, 0.012 and <0.001, respectively). Among the PD subgroups, the mean NLR and CRP levels were statistically similar (all p>0,05) (Table 2).

All of the mean cartilage thickness values of the mild (early) stage PD subgroup were higher than the values of the healthy control group except for the RLFCT. All p values were p<0.001, except for the RLFCT (p=0.217). All of the mean cartilage thickness values of the moderate stage PD subgroup were similar to the values of the healthy control group (all p>0.05). All of the mean cartilage thickness values of the severe PD subgroup were lower than the values of the healthy control group (all p<0.001).

In the mild PD subgroup, all mean cartilage thickness values, except RLFCT, were higher than those in the moderate PD subgroup, and all p values were 0.001, except for the RLFCT (p=0.100). In terms of mean cartilage thickness values, there were higher values in the moderate PD subgroup compared to the severe PD subgroup (all p<0.001) (Table 2).

A strong negative correlation was found between HYS and BBS score (r: -0.943 p<0.001) (Table 3) and between HYS and RADFCT (r: -0.814 pO<0.001) and between HYS and

Table 2. Demographic data and clinical characteristics of Parkinson's subgroups and control group.

		Patient Subgroups			Control Group (n=30)	*p*
		Mild (n=23)	Moderate (n=23)	Severe (n=22)		
Age (years)		63.17 ± 5.86[a]	65.69 ± 5.12[a]	74.59 ± 6.62[b]	66.16 ± 6.16[a]	**< 0.001****
Gender	Female (%)	8 (34.8)	9 (39.1)	10 (45.5)	12 (40.0)	0.910*
	Male (%)	15 (65.2)	14 (60.9)	12 (54.5)	18 (60.0)	
Weight (kg)		84.78 ± 9.73[a]	80.21 ± 7.66[a]	67.90 ± 7.36[b]	80.03 ± 10.11[a]	**< 0.001****
Height (m)		1.67 ± 0.07	1.65 ± 0.10	1.64 ± 0.07	1.66 ± 0.07	0.473**
BMI (kg/m²)		30.33 ± 4.61[a]	29.66 ± 4.15[a]	25.25 ± 2.51[b]	28.71 ± 4.43[a]	**< 0.001****
Disease duration (years)		1.0 (0.1-2.0)[a]	2.5 (1.0-5.0)[b]	8.0 (1.5-20.0)[c]	-	**< 0.001*****
HYS		1.0 (1.0-1.5)[a]	2.5 (2.0-3.0)[b]	4.5 (4.0-5.0)[c]	-	**< 0.001*****
BBS		54 (49-56)[a]	43 (26-51)[b]	3 (0-14)c	-	**< 0.001*****
CRP		4.73 ± 2.11[a]	4.91 ± 2.42[a]	4.98 ± 2.41[a]	2.49 ± 0.96[b]	**< 0.001****
NLR		2.57 ± 0.85[a]	2.60 ± 0.79[a]	2.87 ± 0.62[a]	1.95 ± 0.71[b]	**< 0.001****
RLFCT		2.20 ± 0.19[a]	2.01 ± 0.33[a]	1.43 ± 0.28[b]	2.04 ± 0.26[a]	**< 0.001****
RICNT		2.38 ± 0.30[a]	2.07 ± 0.29[b]	1.48 ± 0.24[c]	1.99 ± 0.20[b]	**< 0.001****
RMFCT		2.44 ± 0.38[a]	1.98 ± 0.21[b]	1.54 ± 0.24[c]	2.02 ± 0.26[b]	**< 0.001****
RADFCT		2.34 ± 0.24[a]	2.02 ± 0.22[b]	1.48 ± 0.18[c]	2.02 ± 0.21[b]	**< 0.001****
LLFCT		2.28 ± 0.30[a]	1.92 ± 0.18[b]	1.48 ± 0.20[c]	1.98 ± 0.17[b]	**< 0.001****
LICNT		2.44 ± 0.33[a]	2.08 ± 0.31[b]	1.47 ± 0.32[c]	2.04 ± 0.18[b]	**< 0.001****
LMFCT		2.29 ± 0.29[a]	1.95 ± 0.17[b]	1.56 ± 0.26[c]	1.99 ± 0.19[b]	**< 0.001****
LADFCT		2.34 ± 0.28[a]	1.98 ± 0.17[b]	1.50 ± 0.21[c]	2.00 ± 0.18[b]	**< 0.001****
R-LADFCT		2.34 ± 0.23[a]	2.00 ± 0.19[b]	1.49 ± 0.18[c]	2.01 ± 0.19[b]	**< 0.001****

*BMI, body mass index; HYS, Hoehn and Yahr scale; BBS, Berg Balance Scale; CRP, C-reactive protein; NLR, neutrophil lymphocyte ratio; RLFCT, right lateral femoral condyle thickness; RICNT, right intercondylar notch thickness; RMFCT, right medial femoral condyle thickness; LLFCT, left lateral femoral condyle thickness; LICNT, left intercondylar notch thickness; LMFCT, left medial femoral condyle thickness; RADFCT, right average distal femoral condyle thickness; LADFCT, left average distal femoral condyle thickness; R-LADFCT, right-left average distal femoral condyle thickness. *Pearson Chi-Square Test, ** One Way ANOVA, *** Kruskal Wallis H Test.*
The difference between the means with different lowercase letters in the same row was found to be statistically significant (p<0.05).

Table 3. Correlations between cartilage thickness, disease severity and balance level.

	HYS		BBS	
	r	*p**	r	*p**
HYS	1.000	.	**-0.943**	**<0.001**
BBS	**-0.943**	**<0.001**	1.000	.
RADFCT	**-0.814**	**<0.001**	**0.802**	**<0.001**
LADFCT	**-0.846**	**<0.001**	**0.812**	**<0.001**

*HYS, Hoehn and Yahr scale; BBS, Berg Balance Scale; RADFCT, right average distal femoral condyle thickness; LADFCT, left average distal femoral condyle thickness. * Spearman correlation analysis, r: Spearman correlation coefficient. *Pearson Ki-Kare Testi. ** Independent Samples t Test.*

LADFCT (r: -0.846, p<0.001) (Figures 3 and 4). A strong positive correlation was found between the BBS score and RADFCT (r: 0.802, p<0.001) and between the BBS score and LADFCT (r: 0.812, p<0.001) (Table 3).

Discussion

While the mean NLR and CRP levels of the PD group were higher than the values of the healthy control group, the mean DFCT values were similar. However, all of the mean cartilage thickness values of the mild stage PD subgroup were higher than the values of the control group except for the RLFCT. Moreover, in the severe PD subgroup, all of the mean cartilage thickness values were lower than the values

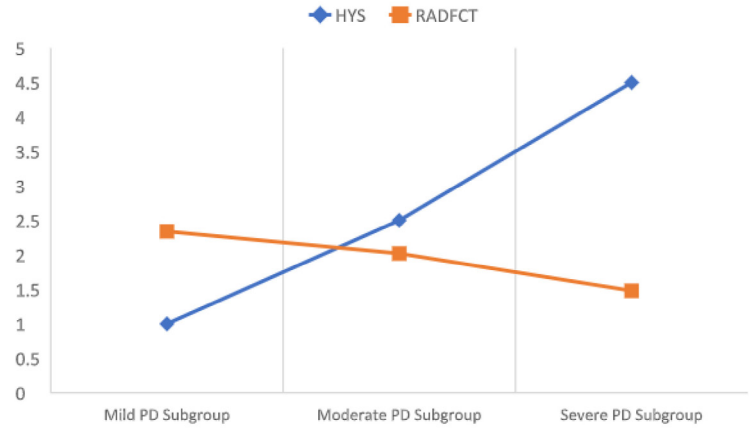

Figure 3. Relationship between RADFCT and HYS.

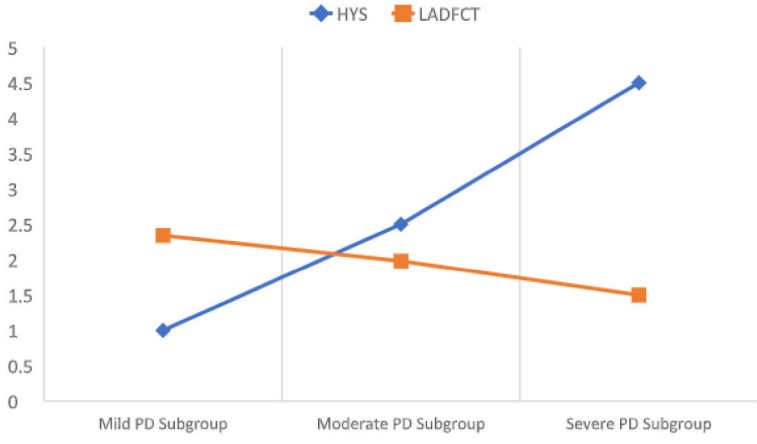

Figure 4. Relationship between LADFCT and HYS.

of the control group. In the moderate stage PD group, mean cartilage thickness values were similar to the values of the control group.

While the mean balance level was good in the mild stage PD subgroup, it was relatively good in the moderate stage PD group. In the severe stage PD subgroup, it was very poor.

The mean age, weight, height and BMI values of the mild stage PD and moderate stage PD subgroups were statistically similar to the mean values of the control group. However, the mean age value in the severe stage PD subgroup was higher than the mean value of the control group, and the weight and BMI values of participants in the severe stage PD subgroup were lower than the values of the control group. Higher mean age was associated with OA progression, while lower weight and BMI were inversely related[11]. It has been shown that weight loss and age increases as the stages of PD progress[12,13].

Recent studies have found an association between OA and PD. In their study published in 2022, Feng et al. showed that the risk of developing PD in individuals with OA was 41% higher than in individuals with similar characteristics without OA[5]. Another study published in 2021 by Jacob et al. showed that this risk had doubled over a 10-year period. Inflammation, lack of physical activity and vitamin D deficiency are the factors that are blamed for the etiology of both PD and OA[1].

The association between OA and inflammation has been demonstrated in recent studies. It has been demonstrated that serum levels of inflammatory mediators such as tumor necrosis factor-alpha (TNF-α) and serum interleukin (IL)-6, which trigger cartilage destruction[14], are high in individuals with OA[15,16]. Local inflammatory cytokines induce cartilage

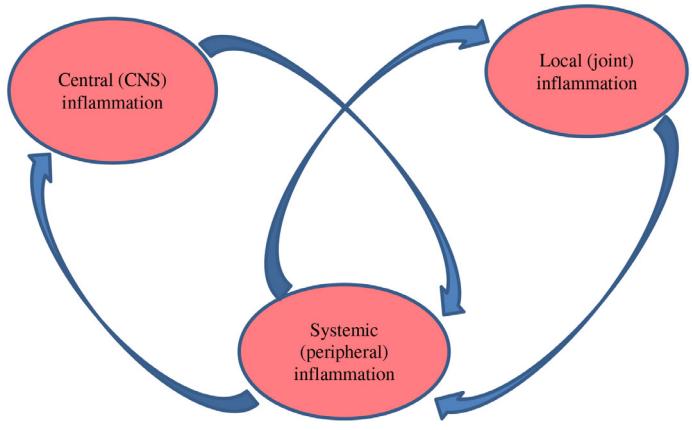

Figure 5. The relationship between central inflammation, systemic inflammation and joint inflammation CNS, central nervous system; Arrows, represent stimulating effect.

degeneration and activate the synovium. Inflammatory events occurring in the joint in patients with OA may also affect extra-articular tissues via blood vessels and may create a peripheral inflammation picture (Figure 5)[17]. However, it has also been shown that systemic low-grade inflammation may activate the development and progression of OA (Figure 5)[17]. OA is now recognized as a disease characterized by low-grade chronic inflammation rather than a degenerative disease. This inflammation, which is shaped by the interaction between metabolic dysfunction, local tissue injury and the immune system, begins to be effective in the early stages of OA. The susceptibility to OA in obese individuals is explained by the excessive load on the joints due to excess weight, as well as excessive adipose tissue-derived systemic mediators (leptin, chemerin, visfatin, resistin, IL-1, IL-6, and TNF-α)[18,19]. In our study, patients in the mild PD group had a mean BMI of over 30, which may have facilitated the triggering of chronic low-level systemic inflammation. In addition to obesity, chronic systemic inflammation associated with PD4 may also contribute to the onset of early signs of OA in the joint[17].

TNF-α and IL-6 may trigger the production of more proinflammatory cytokines by triggering microglia in the brain5. Chronically activated microglia excrete excessive proinflammatory cytokines, thereby increasing inflammation and neurodegeneration. This further stimulates microglia, creating a vicious circle[4].

In patients with PD, the blood-brain barrier deficiencies in the striatum and midbrain were demonstrated through positron emission tomography. Central inflammation in the brain leaks into the systemic circulation due to weakening of the blood-brain barrier (Figure 5)[4]. It has been shown that besides central inflammation, peripheral inflammation can also affect the central nervous system by disrupting the blood-brain barrier (Figure 5)[20]. Peripheral inflammation can activate microglia by weakening the blood brain barrier or affecting the central nervous system via the vagus nerve[4].

TNF-α, IL-6 and IL-1β were found to be high not only in CSF but also in serum in PD. According to the "gut-brain axis" hypothesis, changes in the gut microbiota in PD activate the peripheral inflammatory response, which is characterized by increased cytokine levels and activated T cells[4]. There is increasing evidence that the alteration of gut microbiota is involved in the development of PD through mechanisms such as gut-associated inflammation, weakening of the intestinal barrier, formation of α-synuclein in the gut, and its transport to the brain via the vagus nerve[21]. It has been clearly shown that microbial dysbiosis triggers chronic low-grade inflammation and this inflammation facilitates the development of OA[22]. Moreover, gut microbiota-related Th17 responses have important roles in the etiopathogenesis of both OA and PD[23,24].

NLR is a marker of peripheral inflammation. NLR is a marker that reflects the information of two different sources: the neutrophil (inflammation process) and the lymphocyte (regulatory process). In many studies, it has been suggested that NLR can be used as a biomarker such as acute phase reactants by showing its relationship with systemic inflammation[25,26].

Büyükavcı et al. stated that NLR is a new inflammatory marker that correlates with the radiological severity of knee OA[27]. A meta-analysis published in 2018 showed that patients with knee OA have higher CRP levels compared to healthy individuals[28].

Kara et al. found that the blood NLR level was higher in PD than in healthy individuals[25]. Moreover, a meta-analysis of nine studies also showed that NLR was significantly increased in PD[29]. In many studies, it has been shown that there is a significant increase in blood CRP and hs-CRP levels in PD[26]. In our study, the CRP and NLR values of the patient group were higher than the values of the control group. As a result of our data, we think that the development of OA in patients with PD may be associated with chronic systemic inflammation.

In the current study, the average knee joint cartilage thickness of patients with early-stage PD was thicker than the value of the healthy control group. This situation is a manifestation of cartilage swelling/edema which is a very early indicator of OA[30,31]. On pathological examination and through MRI, it has been shown that cartilage swelling (increase in cartilage thickness) is related to cell death and especially the reduction of matrix proteoglycans[30]. This data was also supported in human studies in which cartilage thickness was evaluated with US[32,33]. This result of our study may provide evidence that early stage PD is releated with OA devolopment.

In our study, cartilage thickness decreased as the PD stage increased, as an indicator of OA progression. Recent studies have suggested that OA increases the occurrence of PD[1,5]. If this process were very common, we should have found the cartilage thickness to be lower in PD patients compared to the healthy control group at each stage, due to possible chronic OA, since OA would develop first and then PD would occur. Since we found findings in favor of early OA in the mild (early) stage PD group in our study, we think that the effectiveness of this hypothesis is weak.

Eckstein et al. determined that there was a significant decrease in cartilage thickness in moderate and end-stage knee OA with MRI[34]. We also found a significant decrease in DFCT in our severe PD disease subgroup. Balance and motor function were very poor in our severe disease subgroup. We think that impaired motor function and balance, as well as inflammation, may contribute to the development and progression of OA. Dysfunctions in neuromuscular factors such as muscle strength and muscle coordination may trigger knee OA by disrupting knee joint stability[35]. However, the balance was quite good in our mild disease subgroup. We think that the increase in DFCT (the earliest sign of OA) at this stage may be associated with peripheral inflammation.

In our transition group (moderate PD disease subgroup), we found the mean DFCT value to be similar to the healthy control group. We think that this is due to the fact that the measurements were made in the transitional PD stage in the process from increased cartilage thickness to decreased cartilage thickness.

Evidence for edema (increase) in cartilage thickness in the Osteoarthritis Research International (OARSI) pathological grading system grade 1 and a decrease in cartilage thickness in OARSI grades 3 and 4 as a result of histopathological sample examinations have been presented in the literature[36,37]. Cartilage pathologies are also shown in grade 2[36]. Unfortunately, our study does not have a histopathological component that shows cartilage pathologies, especially in the transition group (moderate PD disease subgroup).

Early-stage OA is characterized histopathologically by tissue edema, cell death, or cell proliferation (clumping), and cartilage thickness is greater than normal in this period. After the early stage, the secretion of matrix metalloproteinases, aggrecanases, and inflammatory markers increase. As a result of this increased catabolic process, cartilage thickness gradually decreases[37,38].

Our study provides compelling evidence for the development and progression of OA in patients with PD. Studies that will reveal the origin of this relationship between the two diseases at the molecular level may contribute to the development of new treatment strategies. In our study, early and middle-stage PD patients were found to be obese and overweight, respectively. Both PD and OA impair balance and walking[1,2,39]. Prevention of overweight, patient-based exercise program and patient education should be aimed at treatment, even though gait and balance functions are not impaired in the early stage PD. Thus, the development of OA in the early period and the deterioration in balance and walking functions in the later period can be slowed down.

The small sample size of the groups is a relative limitation of our study. The second one is that ultrasonographic measurements were not supported histopathologically. Another limitation of our study was the absence of similarity in some demographic data between PD subgroups and the control group. Age, weight, and BMI were similar between the three groups except for the severe PD subgroup. Age was higher, and weight and BMI were lower in the severe PD subgroup than in the other groups. Although these differences are related to the natural process of the disease, they can cause confounders.

Conclusion

Mean DFCT values in the early-stage PD subgroup were higher than the values of the healthy control group, as a very early sign of OA. In the severe PD subgroup, mean DFCT values were lower than the values of the healthy control group, as an indicator of OA progression. In light of these data, it can be considered that the onset and progression of OA in PD patients may be associated with chronic inflammation.

Ethics approval

Ethical approval of the study was obtained from the ethics committee of Hatay Mustafa Kemal University (Approval No: 03, Date: 04/11/2021).

Consent to participate

A written informed consent form was acquired from the study participants.

Acknowledgement

Murat Güntel lost his life in the great Hatay earthquake on February 6, 2023. With respect to the memory of our dear friend Murat Güntel...

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