

ORIGINAL ARTICLE

Evaluation of the relationship between the anatomical characteristics of the vastus medialis obliquus muscle and the patella chondral lesion occurrence

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Patellar chondral lesions are one of the main causes of anterior knee pain in dissatisfied patients after total knee arthroplasty (TKA).^[1] The presence and development of articular chondral degeneration of the knee joint have been well-known and studied previously.^[2] However, there is no consensus on the etiology of patellofemoral osteoarthritis (PFO), particularly on isolated patellar chondral lesions causing anterior knee pain. Patellofemoral (PF) joint incongruency, lower extremity axial malalignment, and abnormal mechanical or functional characteristics of the surrounding muscles and ligaments of the PF joint are some of the predisposing etiological features that the researchers have focused on.[3-5] The muscles and ligaments of the patella primarily provide stability and secondarily allow a concerted motion in the trochlear groove. By drawing it medially,

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ABSTRACT

Objectives: The study aims to investigate the relationship between the vastus medialis obliquus (VMO) muscle distal insertion features and patellar chondral lesion presence.

Patients and methods: This cross-sectional study included a total of 100 patients (18 males, 82 females, mean age 67.2±7.1 years; range, 50 to 86 years) who underwent total knee arthroplasty (TKA). Radiological assessments, including merchant view and standing orthoroentgenograms, were conducted. The current osteoarthritis stage, varus angle, quadriceps angle (Q angle), patella-patellar tendon angle (P-PT angle), congruence angle, and sulcus angle were calculated. The VMO tendon length, muscle fiber angle, tendon insertion width measurements, and patellar chondral lesion localization data were obtained intraoperatively. Grouping was done according to the distal insertion width of the VMO tendon to the medial edge of the patella. The medial rim of the patella was divided into three equal-sized sectors. The first group (Group 1, n=31) consisted of patients who had an insertion from the quadriceps tendon into the upper one-third of the patella. The second group (Group 1, n=48) consisted of patients with a distal insertion expanding into the middle one-third of the patella. The third group (Group 3, n=21) consisted of patients who had a distal insertion extending into the distal third region of the medial patella margin. The patella joint surface was divided into sectors, and the presence and location of cartilage lesions were noted in detail.

Results: The mean tendon insertion width rate was 45.99±16.886% (range, 16.7 to 83.3%). The mean muscle fiber insertion angle was 51.85±11.67° (range, 20° to 80°). The mean tendon length was 12.45±3.289 (range, 4 to 20) mm. There was no significant difference between the mean age, weight, height, body mass index, BMI, fiber angle, tendon length, varus angle, Q angle, sulcus angle, and congruence angle data among the groups. In terms of the P-PT angle, Groups 1 and 2 had a significant relationship (p=0.008). No relationship was found between the mean fiber insertion angle, mean tendon length, or the presence of chondral lesions. There was a statistically significant difference among the groups regarding the presence of chondral lesions. The highest percentage of chondral lesion frequency was observed in Group 3 (95.24%), followed by Group 1 (90.3%) and Group 2 (89.6%), respectively. Compared to the other two groups, Group 3 had a higher average ratio of lesion areas per patient.

Conclusion: Our study results demonstrate that the formation and localization of the patellar chondral lesions are affected by the insertion width type of the VMO muscle into the patella. Group 2-type insertion is associated with a lower lesion frequency rate than Groups 1 and 3.

Keywords: Articular, cartilage, patella, quadriceps muscle, vastus medialis obliquus.

superiorly, and posteriorly, the vastus medialis muscle and its distal part, the vastus medialis obliquus (VMO) muscle, stabilize the patella against the vastus lateralis (VL) muscle.^[6] Many studies including patients with anterior knee pain have demonstrated that the balance between the VMO and the VL has been distorted in favor of the VL. In this case, VMO atrophy or dysfunction has been blamed as the major pathological condition.^[6,7] However, there are few studies examining the effect of the distal anatomical characteristics of VMO muscle, which may cause PF chondral degeneration. Interestingly, VMO distal anatomical features have also been associated with some other conditions. In their study reports, Koskinen and Kujala^[8] and Gobbi et al.^[9] reported that the VMO insertion was more proximal in patients with patellar instability compared to healthy individuals. In addition, Roberts et al.^[10] observed this in patients with knee osteoarthritis (OA). While a relationship has been shown between instability or tibiofemoral OA in patients with VMO distal insertion type, to the best of our knowledge, there is one study investigating VMO distal anatomical features in the etiology of PFO. This cadaveric study reported a weak correlation between VMO distal anatomical features and patellar cartilage lesions.[11] In the present study, we hypothesized that variations in VMO distal characteristics could impact the degeneration of patellar cartilage at specific localizations. We, therefore, aimed to investigate the relationship between VMO muscle distal insertion features and patellar chondral lesion presence.

PATIENTS AND METHODS

This cross-sectional study was conducted at Hatay Mustafa Kemal University, Tayfur Ata Sokmen Faculty of Medicine, Department of Orthopedics and Traumatology. Individuals aged between 50 and 86 years who underwent unilateral TKA were included in the study. The two surgeons observed each patient (n=196) simultaneously, both preoperatively and intraoperatively, to avoid intra- and interobserver variation. Exclusion criteria included patella alta or baja, congenital or developmental lower extremity deformity, varus deformity greater than 10° or any degree of valgus deformity, history of synovitis or rheumatoid disease, knee musculoskeletal injury, and/or isolated patella chondral damage. Based on the examinations, a total of 100 patients (18 males, 82 females, mean age 67.2±7.1 years; range, 50 to 86 years) were determined to be ineligible for inclusion in the study.

Data including the patient's age, sex, height, weight, and body mass index (BMI) were retrieved from the medical records. Radiological evaluations, such as standing orthoroentgenograms and merchant view radiographs, were carried out. The Mergentech PACS software (Mergentech PACS, Eskişehir, Türkiye) was used to calculate the varus angle, quadriceps angle (Q angle), patella-patellar tendon angle (P-PT angle), congruence angle, and sulcus angle, in addition to the OA stage that is currently present. Data acquisition and measurements were carried out according to the previously described methodologies.^[12-14]

Measurements of the VMO muscle tendon insertion width, length, and muscle fiber angle were performed intraoperatively, along with the patellar chondral observation. The patella and the quadriceps muscles were seen after the anterior median skin incision. A sterile pen was used to draw the landmarks, which included the distal point of the VMO muscle insertion area on the patella, the medial border of the patella, the tendon border, and the direction of the muscle fibers. Measurements were taken using a sterile goniometer and ruler. The ratio of the insertion length to the patella medial border length is used for calculating the VMO insertion width.



The vastus medialis tendon's length was measured from the patella's closest point to the margin of the muscle. Additionally, in the same zone, the tendon insertion angle was measured concerning the femoral anatomical axis (Figure 1).^[11,15]

Following the medial parapatellar or subvastus approach to arthrotomy, patellar articular surface assessments were conducted, and photos were obtained to be saved and reexamined later. To examine the data, grouping of the patients was done according to VMO muscle insertion width by dividing the medial edge of the patella into three equal-sized sectors. The first group (Group 1, n=31) consisted of patients who had an insertion from the quadriceps tendon into the upper one-third of the patella. The second group (Group 2, n=48) consisted of patients who had a distal insertion expanding into the middle one-third of the patella, and the third



group (Group 3, n=21) consisted of patients who had a distal insertion extending into the distal third region of the patella medial margin. The joint surface of the patella is observed by dividing it into two regions: the medial and lateral facet regions. According to our observations during the preparation phase of this study, cartilage lesions were detected in limited areas in many of the patients. For a detailed examination of the joint surface, a division was made into three main horizontal regions: superior, middle, and inferior areas. Then, these regions were divided into three vertical subsections: medial, central, and lateral facet regions. The region containing the patella ridge was the central zone. In total, nine regions were obtained to determine detailed data. It was accepted that areas with cartilage damage in at least 50% of the areas were affected (Figure 2).

Since lesions were detected in more than one region in most patients according to the nine-zone classification, the average ratio of lesion areas per patient was also calculated as a measure of the lesion distribution width of the patients in the groups. This calculation was made as follows: total number of lesion zones detected in the group/number of patients in the group.

Statistical analysis

Statistical analysis was performed using the IBM SPSS version 22.0 software (IBM Corp., Armonk, NY, USA). Continuous data were expressed in mean \pm standard deviation (SD) or median (min-max), while

categorical data were expressed in number and frequency. The Pearson chi-square test and Fisher exact test were used to analyze nominal variables. The one-way analysis of variance (ANOVA) test was used to compare the means within groups, and the *post-hoc* least significant difference (LSD) test was used to analyze the relationship between groups. A *p* value of <0.05 was considered statistically significant.

RESULTS

The arthrotomy type was median parapatellar in 47 patients and subvastus in 53 patients. The operated side was right in 45 and left in 55 knees. No relationship was found between age, weight, height, BMI, fiber angle, tendon length, varus angle, Q angle, and congruence angle parameters with VMO distal characteristics or with chondral lesion presence. However, there was a significant relationship between the groups with the P-PT angle in the one-way ANOVA test. In the *post-hoc* LSD test, this relationship was found to be significant between Groups 1 and 2 (p=0.008) (Table I).

Based on the Kellgren-Lawrence (KL) OA classification, nine out of 31 patients in Group 1, 17 out of 48 patients in Group 2, and five out of 21 patients in Group 3 had Grade 3 OA. In contrast, the remaining patients had Grade 4 OA. Regarding the KL classification, there was no statistically significant difference among the groups (p=0.606).

TABLE I Demographic and baseline data of patient groups								
	Frequency							
Descriptive	Group 1 (n=31)	Group 2 (n=48)	Group 3 (n=21)	Total (n=100)	р			
	Mean±SD	Mean±SD	Mean±SD	Mean±SD				
Age (year)	67±6.398	66.56±7.668	69.05±6.538	67.22±7.063	0.400			
Height (cm)	167.68±6.068	165.73±7.434	165.95±7.704	166.38±7.082	0.472			
Weight (kg)	83.94±8.880	82.33±10.584	80.19±11.531	80.38±10.282	0.440			
Body mass index (kg/m ²)	29.83±3.125	29.94±3.381	29.01±2.716	29.71±3.164	0.525			
Fiber angle (°)	54.52±10.674	50.63±11.652	50.71±12.97	51.85±11.67	0.313			
Tendon length (mm)	12.84±3.338	12.21±2.76	12.43±4.308	12.45±3.289	0.711			
Varus angle (°)	7.2±2.687	6.55±2.049	6.72±2.332	6.79±2.315	0.476			
Q angle (°)	11.33±4.85	12.52±5.368	12.24±4.837	12.09±5.08	0.596			
P-PT angle (°)	143.98±6.161	147.46±4.869	145.31±6.274	145.93±5.756	0.026			
Sulcus angle (°)	136.83±12.01	134.98±10.93	131.22±12.04	134.76±11.56	0.228			
Congruence angle (°)	12.35±3.868	13.72±3.532	12.32±4.211	13.01±3.811	0.194			
SD: Standard deviation.								



The mean tendon insertion width rate was $45.99\pm16.886\%$ (range, 16.7 to 83.3%). The patients' tendon length and angle variables were in a normal distribution. The mean muscle fiber insertion angle was $51.85\pm11.67^{\circ}$ (range, 20 to 82°). The mean tendon length was 12.45 ± 3.289 (range, 4 to 22) mm. There was no significant difference in the mean muscle fiber insertion angle and tendon length data among the groups (Table I).

Only 39% of the patients had chondral lesions on the lateral side, compared to 96% who had lesions on the medial side. In addition, 55% of the patients had central zone lesions. A total of 2% of the patients had isolated lesions in the central ridge, and 32% had isolated medial lesions. Nevertheless, no isolated lateral lesion was detected. Also, lesions were found in the superior zone in 45% of the patients, the middle zone in 93%, and the inferior zone in 37% of them.

The highest percentage of total chondral lesion frequency was observed in Group 3 (95.2%) (n=20/21) followed by Group 1 (90.3%) (n=28/31) and Group 2



(89.6%) (n=43/48), respectively. The average ratio of lesion areas per patient was 5.29 in Group 3, while it was 2.68 in Group 1. Group 2 had the lowest ratio at 2.10.

Total chondral lesion frequencies according to localizations in the cohort are shown in Figure 3. The distribution of the chondral lesion frequencies according to groups is shown in Figure 4.

A statistically significant relationship was observed between Groups 1 and 3 and the location

of the chondral lesions in specific zones. However, in Group 2, there was no statistically significant relationship (Figure 3, Figure 4, Table II).

The data evaluations for male and female patients are presented in Table III. No significant differences were noted while comparing male and female data except for height and BMI mean values. A total of 51 of the female patients had lesions on the medial side and 32 on the lateral side. Seven and 15 of the male patients showed lateral and medial chondral lesions, respectively.

TABLE II Comparison of localization frequencies of chondral lesions								
	Lesion frequency							
	Group 1	Group 2	Group 3	Total	p			
Chondral lesion location zone	%	%	%	n				
Superior medial	74.2	14.6	66.7	44	0.000			
Middle medial	80.6	87.5	95.2	87	0.125			
Inferior medial	12.9	29.2	81	35	0.000			
Superior central	19.4	0	14.3	9	0.307			
Middle central	35.5	45.8	85.7	51	0.001			
Inferior central	3.2	6.3	57.1	16	0.000			
Superior lateral	22.6	0	19	11	0.398			
Middle lateral	9.7	29.2	52.4	28	0.003			
Inferior lateral	0	0	23.8	5	0.000			

	TABLE III							
Demographic and baseline data of patients according to sex								
Sex	Female (n=82)	Male (n=18)	Total (n=100)					
Descriptive	Mean±SD	Mean±SD	Mean±SD	p				
Age	66.7±6.623	69.61±8.61	67.22±7.063	0.113				
Height	165.62±7.064	169.83±6.243	166.38±7.082	0.022				
Weight	82.51±10.546	81.78±9.233	80.38±10,282	0.785				
Body mass index	30.06±3.292	28.13±1.846	29.71±3.164	0.018				
Insertion width (%)	46.51±17.106	43.49±16.047	45.99±16.886	0.495				
Fiber angle	52.44±11.66	49.17±11.663	51.85±11.67	0.284				
Tendon length	12.27±3.274	13.28±3.322	12.45±3.289	0.240				
Varus angle	6.84±2.404	6.58±1.905	6.79±2.315	0.668				
Q angle	11.80±4.926	13.45±5.683	12.09±5.08	0.212				
P-PT angle	146,27±6,171	144,36±2,879	145.93±5.756	0.204				
Sulcus angle	133.97±11.722	138.37±10.354	134.76±11.564	0.145				
Congruence angle	12.77±3.782	14.09±3.866	13.01±3.811	0.184				
SD: Standard deviation; P-PT: Patella-patellar tendon.								

DISCUSSION

The results of the present study revealed that the type of insertion width of the VMO muscle affected the formation and location of patellar chondral lesions. Patients in Groups 1 and 3 displayed statistically significant chondral lesions at specific facet zones. However, there was no statistically significant relationship observed in Group 2 and the occurrence of chondral lesions at specific localizations. The prevalence of chondral lesions in Group 3 was quite high in all joint surface areas, except for the superior medial, superior central, and superior lateral joint surfaces, which were shown to have the highest incidence of cartilage lesions in Group 1. Compared to the other groups - 5.29 in Group 3, 2.68 in Group 1, and 2.10 in Group 2 - Group 3 had a higher average ratio of lesion areas per patient. Nevertheless, it failed to be possible to demonstrate any relationship between tendon length or fiber angle and the occurrence of patellar chondral lesions.

Although experiences may differ, the literature has recognized the significance of data such as Q angle, P-PT angle, sulcus angle, and compliance angle as signs of multiple factors that may cause the onset and progression of PFO. Since there was no control group in our study, we were only able to compare the data among the groups, even though our results were in the range that was mentioned in the literature.^[16-21] In contrast to Erduran et al.'s^[20] study, which examined the PF joint dynamics of patients with tibiofemoral OA, the mean congruence angle was a little higher in our study; nevertheless, the mean sulcus angle and Q angle were comparable.

Aksahin et al.^[21] examined the possibility that sagittal patellar tilt could be a factor for cartilage lesion occurrence in various locations. They reported that the mean P-PT angle in the group with chondromalacia was significantly lower than that of the control group. The P-PT angle did not statistically significantly differ between the control group and the patients with middle-zone cartilage defects. Nonetheless, in contrast to middle-zone cartilage defects and to the control group, the mean P-PT angles in patients with superior (141.8±2.7) and inferior (139.2±2.3) cartilage defect subgroups were significantly lower. In line with the findings of Akşahin et al.,[21] we also observed that patients in Group 1, who had more frequent lesions in the superior region, and Group 3, who had more frequent lesions in the inferior region, had lower P-PT angles than patients in Group 2.

According to Rajput et al.,^[22] the mean VMO muscle fiber insertion angle was 41.26° (range, 46° to 56°), which Holt et al.^[23] reported as 43° (range, 30° to 60°). However, Hubbard et al.^[24] and Peeler and Anderson^[11] reported a higher value of 53.2° (range, 28° to 70°) and 57° (range, 50° to 70°), respectively. In addition, in their study, Pagnano et al.^[15] observed the patients during TKA surgery and reported that the mean angle of VMO insertion was 50° (range, 46° to 52°). The distribution width (range, 20° to 80°) was large, but the mean fiber angle was 51.85° in our cohort, within the range reported by previous studies. The comprehensive examination revealed no correlation between fiber angle and groups, nor between the occurrence of chondral lesions in certain zones.

There are not sufficient publications regarding VMO tendon length in the literature. In a cohort consisting of 45 cadaveric specimens, 100 patients, and five normal volunteers, Pagnano et al.^[15] showed a bimodal distribution of VMO tendon length. They observed that the mean tendon length (1.2 ± 0.1 cm) was significantly short in 100 out of the 150 knees they studied (66%). A relatively long tendon with an average length of 2.2±0.2 cm was present in 50 of the 150 knees (33%). Furthermore, the mean tendon length of the patients (n=100) that they assessed intraoperatively during TKA was 14 mm, which was greater than what we found in our study.

Holt et al.^[23] reported that the mean insertion width rate of the VMO tendon was 51% (range, 13 to 95). Similarly, Pagnano et al.^[15] found a mean insertion rate of 50% (range, 45 to 55%). In another study report, Roberts et al.^[10] found that most of the patients (79.7%) had an insertion width that terminated in the proximal half of the patella. Chavan and Wabela^[25] reported that 20% of cases had insertion on one third proximal, 62.5% on two third proximal, and 17.5% on the entire patella. In our study, the mean distal insertion width rate of the VMO tendon was below average compared to previous studies (45.99%; range, 16.7 to 83.3%). Totally, 31% of cases had insertion on the one third proximal, 48% on the two third proximal, and 21% on the entire patella. In addition, 75% of the patients had a termination in the proximal half of the patella, and a whole margin insertion into the patella was not detected. It was thought that these differences in rates, which were partially different from the literature, might be due to racial characteristics. In particular, our results support the view that, as mentioned previously, a significant portion of patients planned for mini-subvastus arthrotomy would not be suitable for this strategy.^[15]

Many researchers have indicated that degenerative cartilage lesions of the patella are typically located on the medial facet rather than the lateral.^[19,26] In line with previous research, patellar chondral lesions were most commonly seen on the medial side in the present study. In their study, Iriuchishima et al.^[19] reported that only 2% of patients had OA on the patella's lateral facet. Furthermore, they noted a significant amount of cartilage erosion in the patellar facet globally, as well as in the central ridge region. In our study, there were no isolated lateral facet chondral degenerations, and only two patients had isolated central region lesions. Regarding region-based chondral lesion mapping, our research provides additional information on a significant aspect that has not received much attention in the literature.

During active motion, the location of the patella in the femoral trochlea changes; the contact area and the amount of load on the articular cartilage are altered by the medial, superior, and posterior pulling forces of the VMO.^[6,27] Therefore, VMO insertion width may have an impact on the movement and rotation of the patella, and this may be an important cause for more frequent chondral lesion occurrences in different locations. As a result, we thought that this was the reason for the different average ratio of lesion areas per patient in the groups and the lesion occurrence areas specific to the groups.

To the best of our knowledge, there is only one study in the literature conducted by Peeler and Anderson^[11] that analyzed the relationship between VMO distal characteristics and the distribution of patellar chondral degeneration.^[11] In this cadaveric study (n=32, mean age: 79±12 years), Peeler and Anderson^[11] reported that the majority of cartilage lesions were located in the medial facet of the patella, particularly in the middle medial facet region. However, they found no significant relationship between the fiber insertion angle and insertion width parameters of VMO and patellar cartilage lesion formation. Our results are consistent with the Peeler and Anderson's^[11] results indicating that patellar lesions were more common in the middle part of the medial side. However, we found a relationship between the insertion width and cartilage lesion occurrence, although not in the tendon length and fiber angle measurements of our patients. Another distinction is that we found lateral cartilage lesions in 39% of our patients and medial cartilage lesions in 96% of them. Peeler and Anderson^[11] reported rates

that were somewhat close to each other, at 65% and 61%, respectively. In addition, Peeler and Anderson^[11] found that the mean fiber insertion angle value, as well as the mean insertion width value, in females were smaller than in males. In our cohort, although the measurement results were not statistically significant, they were found to be greater in males. These different results we obtained may have been due to racial characteristics or, undoubtedly, some discrepancies in our study design. The fact that nearly half of their patients had alignment issues and all of our patients had advanced-stage tibiofemoral OA could have been responsible for this. Unlike Peeler and Anderson,^[11] we observed many more patients during TKA surgery. We analyzed a more homogeneous group that did not have knee and patella alignment problems such as varus over 10° or any degree of valgus. However, in the 32 lower extremities of the 24 cadavers examined in the study by Peeler and Anderson,^[11] 17 were normal, 12 had valgus, and two had varus deformities. In our study, different from theirs, we calculated the ratio of insertion width to patella medial edge length to avoid the error of measuring the insertion width parameter due to the different patella sizes in the patients.

Anterior knee pain is an important health problem for all ages. Although many publications have shown that the effect of patellar cartilage status on functional results after TKA and unicompartmental knee arthroplasty is significant or vice versa, the patient factors causing both results or the underlying cause are unknown.^[26,28] Furthermore, there is no consensus on the most optimal approach for the treatment of patients with PF arthritis based on studies that have shown positive outcomes.^[2,29,30] Some authors have reported remarkable negative changes in areas with patellar cartilage damage in various situations, such as the surgical results of patellar subluxation or luxation. Consequently, several of these techniques are not favored by surgeons.^[31] In a remarkable study report, Pidoriano et al.^[32] reported that tibial tubercle transfer surgery, making an axis change, had a significant effect on the clinical results of patients who had patellar joint cartilage lesions. These results were significantly correlated with the localization and severity of the cartilage lesions. In addition, the effect of vastus medialis augmentation on PF degeneration and anterior knee pain has been demonstrated after procedures for patellar instability or maltracking treatment. It is noteworthy that successful clinical results were achieved with various extensor mechanism rearrangement surgeries based

on the Insall's proximal realignment procedure.^[33,34] According to these findings, it may be possible to inhibit cartilage degeneration or delay the progression of chondral injury in particular zones by altering the VMO distal insertion and, as a result, altering the stress vectors on the patella. In the future, new procedures for the treatment of patellar chondral lesions that correlate with VMO distal features can be planned in light of these findings.

Nevertheless, there are some limitations to this study. First, we examined the patients during the routine TKA surgery procedure and, therefore, we were unable to perform some further alignment evaluations that could have been done using computed tomography (CT) or magnetic resonance imaging (MRI). In addition, we were unable to perform various dynamic radiological examinations on our patients. Therefore, despite our attempts to examine the patellar chondral surface and VMO, the impact of knee motion, VL, and VMO kinematics on the status of daily living activities was not considered to shed light on the etiological effect of chondral lesion formation. Furthermore, since all of our patients had severe tibiofemoral OA, it is necessary to generalize these findings to healthy individuals and patients with isolated PFO at similar and younger ages. On the other hand, the main advantages over previous studies include the use of direct measurements and observations of the VMO muscle and patella articular surface during TKA surgery rather than CT or MRI.[35] Another advantage is that we studied with a more homogeneous group with fewer alignment issues. Our research highlights significant details that provide another perspective on the etiology of PFO.^[35] Thus, this can address new research about a novel and safe modification technique based on the transfer of the VMO insertion site that can restore the PF joint dynamics, prevent the development of cartilage lesions, and treat PFO.

In conclusion, our study results demonstrate that the formation and localization of the patellar chondral lesions are affected by the insertion width type of the VMO muscle into the patella. Group 2-type insertion is associated with a lower lesion frequency rate than Groups 1 and 3. Further studies are warranted to confirm these findings.

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Ethics Committee Approval: The study protocol was approved by the Hatay MKÜ Tayfur Ata Sökmen Faculty of Medicine Clinical Research Ethics Committee (date: 03.05.2020, no: 2020/49). The study was conducted in accordance with the principles of the Declaration of Helsinki.

Patient Consent for Publication: A written informed consent was obtained from each patient.

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

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