ORIGINAL ARTICLE

PLATELET RICH PLASMA RESULTS IN THE TREATMENT OF FEMUR HEAD AVASCULAR NECROSIS

Femur Başı Avasküler Nekroz Tedavisinde Trombosit Zengin Plazma Sonuçları

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ABSTRACT

Objective: It has been observed that the number of patients with hip avascular necrosis who applied to our clinic after Covid-19 and steroid treatment in Covid-19 treatment has increased. It is emphasized in the literature that core decompression therapy is effective in early stage femoral head avascular necrosis. Core it has been emphasized in many publications that the results of intraoperative platelet- rich plasma (PRP) application after decompression are effective. However, intraoperative the method of application of platelet- rich plasma (PRP) and its effectiveness in the post-Covid-19 period are not emphasized enough in the literature. The aim of this study is to evaluate the effect of local platelet-rich plasma (PRP) administered using the new technique after core decompression to patients diagnosed with avascular necrosis.

Material and Methods: Local platelet- rich plasma (PRP) was applied to 15 hips diagnosed with femoral head avascular necrosis after core decompression with a new technique. Early results of the patients were evaluated with Ficat and Harris hip scores.

Results: An improvement was detected in the early clinical and Magnetic resonance (MR) findings of a total of 15 hip avascular necrosis patients. Local treatment in patients with avascular necrosis with a medical history of Covid-19 the feasibility of PRP was demonstrated.

Conclusion: This study shows the importance of the intraoperative application method of platelet- rich plasma (PRP) and that platelet- rich plasma (PRP) can also be applied to Covid-19 patients. But we believe long-term results are needed.

Keywords: *Femoral Head Necrosis; Osteonecrosis; Steroids; COVID-19; Platelet Rich Plasma*

ÖZET

Amaç: Covid-19 ve Covid-19 tedavisinde steroid tedavisi sonrası kliniğimize başvuran kalça avasküler nekrozlu hasta sayısının arttığı gözlenmiştir. Literatürde erken evre femur başı avasküler nekrozunda kor dekompresyon tedavisinin etkili olduğu vurgulanmaktadır. Core dekompresyonu sonrası intraoperatif uygulanan trombositten zengin plazma (PRP) uygulamasının sonuçlarının etkili olduğu birçok yayında vurgulanmıştır. Ancak intraoperatif trombositten zengin plazmanın (PRP) uygulanma yöntemi ve Covid-19 sonrası dönemdeki etkinliği hakkında literatürde yeterince vurgulanmamaktadır. Bu çalışmanın amacı, avasküler nekroz tanısı alan hastalara uygulanan core dekompresyon sonrası yeni teknik kullanılarak verilen lokal trombositten zengin plazmanın (PRP)'nin etkisini değerlendirmektir.

Gereç ve Yöntemler: Femur başı avasküler nekroz tanısı alan 15 kalçaya core dekompresyonu sonrası trombositten zengin plazmanın (PRP)'nin etkisini artırmak amacıyla yeni bir teknikle lokal PRP uygulandı. Hastaların erken dönem sonuçlarını Ficat ve Harris kalça skorlarıyla değerlendirildi.

Bulgular: Toplam 15 kalça avasküler nekrozu olan hastaların erken klinik ve Manyetik rezonans (MR) bulgularında iyileşme saptandı. Tıbbi geçmişinde Covid-19 bulunan avasküler nekrozlu hastalarda lokal PRP'nin uygulanabilirliğini ortaya koyuldu.

Sonuç: Bu çalışma PRP'nin intraoperatif uygulama yönteminin önemini ve trombositten zengin plazmanın (PRP) Covid-19 hastalarında da uygulanabileceğini göstermektedir. Ancak uzun vadeli sonuçlara ihtiyaç olduğuna inanıyoruz.

Anahtar Kelimeler: *Femur Başı Nekrozu; Osteonekroz; Steroidler; COVİD-19; Trombositten Zengin Plazma*

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INTRODUCTION

Covid-19 and steroid treatment during Covid-19 treatment have been shown in various studies to be an etiology of femoral head avascular necrosis. In the post-Covid-19 period, it has been observed that the incidence of hip avascular necrosis has increased in patients treated with Covid-19 (1, 2).

Osteonecrosis is the process of bone death that can be associated with poor circulation due to a variety of factors. It occurs as venous stasis and arterial occlusion due to circulatory disturbance, vascular endothelial damage and microvascular thrombosis (3, 4). Increased intramedullary adipogenesis in the bone structure after circulatory disturbance, increased osteocyte apoptosis, increased osteoclasts and decreased osteoblast production cause the bone death process (5). When the bone death process occurs as a result of pathology of the vessels supplying the femoral head, it is called avascular necrosis of the femoral head. The etiology of femoral head avascular necrosis is divided into two basic groups: traumatic and non-traumatic. Traumatic etiologies include fractures, dislocations, vascular injuries and previous surgery. Non-traumatic etiologies are a very large subgroup. These include systemic steroid use, pregnancy, alcohol, smoking, systemic diseases (coagulopathies, polycythemia, sickle cell anemia, metabolic diseases, gastrointestinal diseases (Crohn's disease, ulcerative colitis), organ transplantation and radiation exposure (6-8). In addition, in the post-Covid-19 era, studies have shown that Covid-19 and steroid therapy given in the treatment of Covid-19 have a role in the etiology of avascular necrosis (1, 2).

Diagnosis of ONFH (osteonecrosis of the femoral head) includes plain radiography and magnetic resonance imaging (MRI). MRI is up to 100% sensitive for diagnosis (9). The presence of a subchondral fracture on imaging indicates disease progression and may help guide treatment. Successful treatment depends on accurate staging. Various classification systems have been defined for avascular necrosis of the femoral head (10). The one of them is Ficat classification system (11).

ONFH typically follows a progressive course and most untreated lesions lead to irreversible collapse (12). For ONFH prior to collapse (irreversible collapse), core decompression (CD) procedures are recommended to protect and treat the femoral head (13).

Oedema only occurs after blood flow has stopped due to occlusion of the vein in the femoral head. This oedema increases the pressure within the femoral head, suppressing blood flow in the unobstructed vessels, slowing it down and even causing it to clot and close. Core decompression surgery technically involves opening multiple or single tunnels into the oedematous area (14). This reduces the pressure caused by the oedema in the femoral head and allows the pressurized veins to carry more blood.

Recently, many publications have emphasized that intraoperative platelet rich plasma (PRP) treatment is applied locally after nucleus decompression and that the results are effective (15). In the literature, it is emphasized that the method of application, which we believe is one of the most important stages in the effectiveness of PRP, is performed using a 3-way cannula with a needle or a long spinal needle under the guidance of the trocar used in biopsies (16). However, as these methods are not long enough to reach the necrosis area, we develop the long needle catheter method and apply PRP. The aim of the new technique is to increase the concentration of PRP applied locally to the treatment area, thereby increasing the success of the treatment.

In our study, we aimed to evaluate the early results of PRP treatment using our own technique after core decompression in patients with femoral head avascular necrosis who presented to our clinic in the post-Covid-19 period.

MATERIALS AND METHODS

The study was approved by the Ethics Committee of the University of Bozok University with the number 2024-GÖKAEK-242_2024, 04, 24_08. The initial results of PRP applied with our own technique after core decompression in 15 hips of 11 patients diagnosed with avascular necrosis were evaluated.

None of the 11 patients included in the study had a history of avascular necrosis due to trauma. 4 of the patients had a history of covid-19. 1 in 4 patients with a history of Covid-19 had received steroid treatment. Three patients had a history of steroid use for other reasons. No etiological factor was found in 4 patients. The study used the Ficat avascular necrosis staging

system (11). The Ficat-Arlet staging system basically consists of 5 stages.

Stage 0: This is the stage when clinical and radiographic findings are normal.

Stage 1: This is the stage when there is hip pain but no radiographic findings. (MRI and scintigraphy findings may be positive at this stage).

Stage 2: It represents the pre-collapse repair phase, in which the shape of the femoral head is not distorted and the joint space is preserved. There is diffuse increased porosity, areas of demineralization in the form of cystic changes and patchy sclerosis.

Stage 3: This stage represents early collapse and flattening of the femoral head. A linear subchondral lucency (crescent sign) representing the fracture line just below the articular surface is seen at this stage. The joint space is preserved.

Stage 4: Loss of the smooth convex contour of the femoral head and its flattening, collapse and severe collapse of the femoral head; narrowing of the joint space, marginal osteophyte formation and subchondral cyst formation constitute the process leading to progressive degenerative joint disease. Cystic lesions may occur in sclerotic areas and are associated with a poor prognosis (17).

Harris scoring was used in the clinical follow-up of patients. The Harris scoring consists of four subsections: pain (1 question; maximum 44 points), function (7 questions; maximum 47 points), deformity (1 question; maximum 4 points), and normal joint motion (1 question; maximum 5 points). The maximum score that can be obtained from the survey is 100. A high score indicates a good outcome. Scores between 90 and 100 points are considered 'excellent', scores between 80 and 89 points are considered 'good', scores between 70 and 79 points are considered 'fair' and scores below 70 points are considered 'poor' (18).

For retrospective patient outcomes, pre- and post-operative information of patients diagnosed with avascular necrosis who presented with hip pain to Bozok University Faculty of Medicine between 01.06.2017 and 01.03.2024 were accessed. The study is retrospective, and permission was obtained from the chief physician to collect data without informed consent from the patients.

Surgical technique: An Albe table was used for surgery after anesthesia. A Kirschner wire (1.8 mm x 30 cm), a drill that could go over the wire (4 mm x 22.5 cm), a Nelaton catheter (4 mm (12 CH) x 50 cm) for PRP injection and 5 cc syringes for PRP application were used for surgery (Figure 1).

A Kirschner wire entry point was determined from the patient's lateral hip under scope. The areas of intense femoral head avascular necrosis were then identified on AP and lateral scope images and a Kirschner wire was sent to these areas (Figure 2). The avascular area was perfused through decompression by drilling over the Kirschner wire. When the drill was removed, care was taken not to take the Kirschner wire with it (Figure 2). Prior to surgery, the length of the K-wire was used as a reference and the length of the Nelaton catheter was adjusted to match the length of the Kirschner wire (Figure 2). After the Nelaton catheter was passed over the Kirschner wire, the Kirschner wire and Nelaton catheter were held in place with different clamps to ensure that the Nelaton catheter was not pulled during removal of the Kirschner wire (Figure 2).

After surgery, 10 cc of blood was drawn from the patient. In accordance with PRP application principles, care was taken not to shake the tube from which the blood was drawn and to apply it within the first 10 minutes (19).

Five cc of PRP, produced as a result of 3200 rpm for 15 minutes in the centrifuge, was applied to the blood-filled area through a Nelaton catheter (Figure 2). Immediately after PRP application, the aim was to apply isotonic fluid up to the internal volume of the catheter (2 cc) through the Nelaton catheter to prevent retrograde leakage of PRP (Figure 3) and apply it to the AVN area with full efficiency (Figure 2). The Nelaton catheter was then removed and the fascia and subcutaneous tissue were closed with 2/0 Vicryl and the skin with 2/0 Prolene. The patient was discharged the following day. He was seen for weekly follow-up.

Statistical Analysis

The programme "IBM SPSS Statistics for Windows, version 26.0" was used to analyze the data obtained. (IBM Corp. Released 2019. IBM SPSS Statistics for Windows, Version 26.0. Armonk, NY: IBM Corp.) The demographic information of individuals is presented as frequencies (n) and percentages (%).

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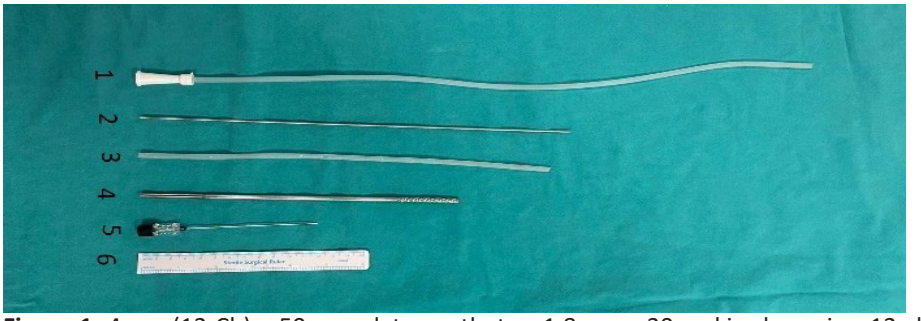

Figure 1. 4mm (12 Ch) x 50cm nelaton catheter ,1.8mm x 30cm kirscher wire ,12-ch nelaton catheter , length matched to the K-wire, 4 mm drill, spinal needle used in other studies, length gauge, note that the length of the spinal needle is shorter than the nelaton catheter.

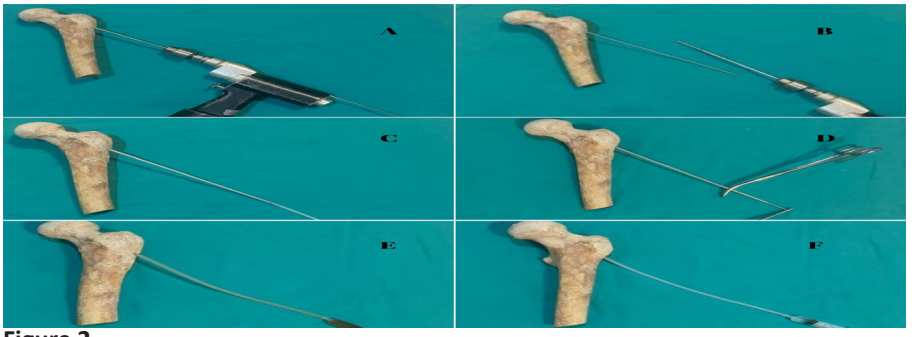

Figure 2.

A-Sending the drill over the Kirschner wire and preventing the Kirschner wire inside from coming back when the drillis removed.

B-Sending the Kirschner wire, which is a guide for the left femoral drillis.

C-Visualisation of the difference in length after sending the Kirschner wire of the normal (not shortened) Nelaton catheter.

D-After the Nelaton catheter is sent over the Kirschner wire, the Kirschner wire and the Nelaton catheter are held with different clamps, and the Nelaton catheter is not removed while the Kirschner wire is removed.

E-Platelet rich plasma application.

F-Platelet rich plasma application, isotonic fluid is sent through the Nelaton catheter to fill the internal volume of the catheter (2 cc) to prevent retrograde flow of platelet rich plasma and deliver it to the avascular necrosis area with full efficiency.

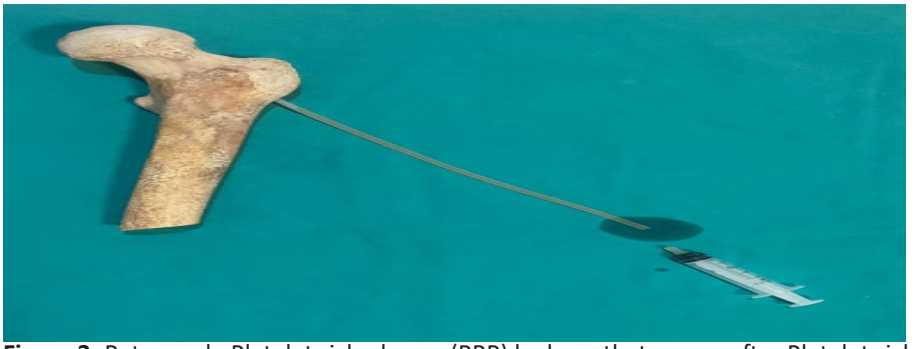

Figure 3. Retrograde Platelet rich plasma (PRP) leakage that occurs after Platelet rich plasma (PRP) application if not enough fluid is sent into the Nelaton catheter (2cc).

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The Shapiro-Wilk normality test was used to determine that the data did not conform to a normal distribution. The Wilcoxon Signed Rank Test was used to determine the differences between the pre- and post-assessment. The power analysis of the study was performed using G*Power 3.1.9.4 and the effect size (dz) based on the Ficat scores of 15 hips evaluated with the Wilcoxon Signed Rank Test was calculated to be 0.92. Based on this effect size, it was determined that the test performed with 15 hips had 90% power. Statistical significance was accepted as $p<0.05$.

RESULTS

Medical histories were obtained from 15 patients diagnosed with hip avascular necrosis. Of the 11 patients, 6 females and 5 males, 7 were diagnosed with unilateral hip avascular necrosis and 4 were diagnosed with bilateral hip avascular necrosis.

Direct radiographs and MRI scans of the hip were obtained during the patients' admission and follow-up. Avascular necrosis of the femoral head was observed on magnetic resonance (MR) imaging in patients whose radiographs showed no features. On MRI images, 1 hip was graded FICAT stage IV, 9 hips were graded FICAT stage III, 4 hips were graded FICAT stage II, and 1 hip was graded FICAT stage I. Preoperative Harris hip scores were graded good in 1 hip, fair in 2 hips, and poor in 12 hips. These patients were treated with PRP using the new technique after core decompression.

Sutures were removed on the 15th day of patient follow-up. There was a significant improvement in hip scores and a significant decrease in pain medication use in 5 patients at 3 months post-operatively. Ficat scores on MRIs at 3 months post-operatively and Harris hip scores, which indicate clinical improvement, were evaluated (Table 1).

In the Harris score evaluation of 11 patients at the 3rd postoperative follow-up, 7 hips were considered fair, 6 hips were considered good and 1 hip was considered excellent. In the control MRI images, 1 hip was graded FICAT stage III, 13 hips were graded FICAT stage II and 1 hip was graded FICAT stage I.

Harris scores increased in 13 patients. Harris scores decreased in 2 patients. The Ficat score decreased in 10 patients and remained constant in 5 patients (Figure 4).

In the Harris score evaluation of 4 patients at the 3rd postoperative follow-up, 1 hip had an excellent score, 2 hips had a good score, and 4 hips had an average score. In the control MRI scans, 6 hips were classified as FICAT

Table 1. Comparison of patients' preoperative Harris and Ficat scores and postoperative Harris and Ficat scores. Harris scoring consists of 0-40 poor, 41-60 fair, 61-70 good, 71-85 very good, 85-100 excellent and Ficat-Arlet staging system consists of 5 stages: 0-4.

	Preoperative harris score	Preoperative MRI	Postoperative 3rd month Harris score	Postoperative 3rd month MRI
Patient 1-Right	**29**	**3**	**51**	**2**
Patient 1-Left	**27**	**3**	**49**	**2**
Patient 2-Right	**26**	**3**	**69**	**2**
Patient 2-Left	**51**	**2**	**70**	**2**
Patient 3-Right	**31**	**1**	**49**	**1**
Patient 3-Left	**69**	**2**	**86**	**2**
Patient 4-Left	**40**	**3**	**57**	**2**
Patient 5-Right	**32**	**3**	**70**	**2**
Patient 5-Left	**45**	**3**	**42**	**2**
Patient 6-Right	**40**	**4**	**69**	**3**
Patient 7-Left	**28**	**3**	**42**	**2**
Patient 8-Right	**30**	**3**	**57**	**2**
Patient 9-Left	**28**	**2**	**68**	**2**
Patient 10-Right	**30**	**3**	**70**	**2**
Patient 11-Left	**29**	**2**	**27**	**2**

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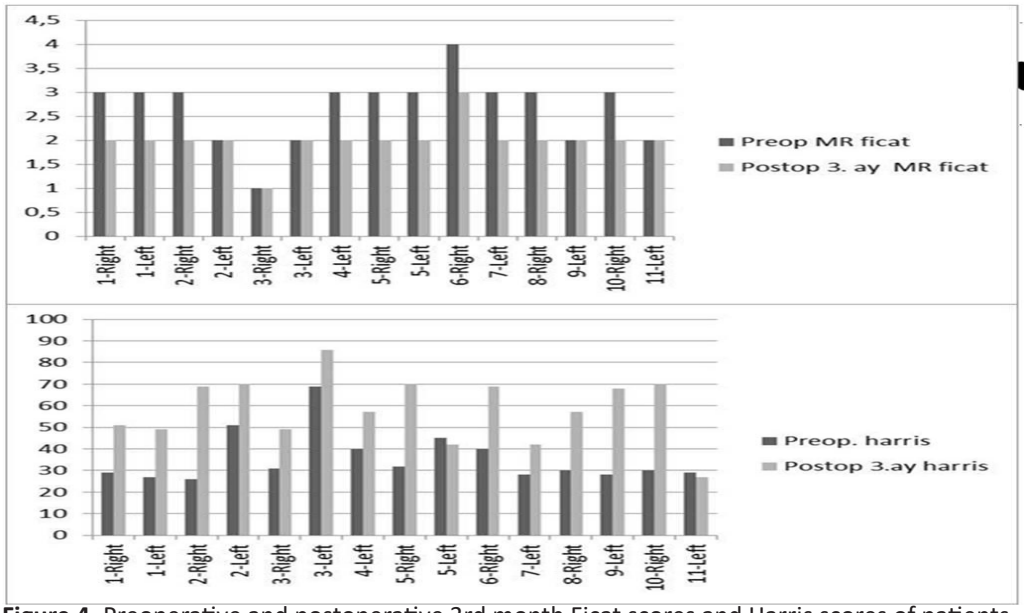

Figure 4. Preoperative and postoperative 3rd month Ficat scores and Harris scores of patients.

Table 2. Wilcoxon signed ranks test results and medians (Q1-Q3) of Ficat and Harris scores.

	Preop	**Postop**	z	P
	Median (Q1-Q3)	Median (Q1-Q3)		
Harris Score	30 (28-40)	57 (49-70)	-3,239	**0,001***
Ficat	3 (2-3)	2 (2-2)	-3,162	**0,002***

stage II and 1 hip was classified as FICAT stage I (Table 2).

DISCUSSION

In our study, we tried to develop different perspectives on the treatment of avascular necrosis of the hip. Firstly, we have demonstrated the applicability of PRP in patients who have undergone Covid-19 in the post-Covid-19 period. Secondly, we emphasized and tried to improve the method of application of intraoperative PRP in patients undergoing cord compression.

There are various studies on the drilling method and the importance of the material applied in the treatment of femoral head avascular necrosis (13). However, we believe that the injection method is also important in post-drill PRP treatment.

In the animal study conducted by Zhang et al, PRP application was tried in femoral neck fractures and they stated that they applied PRP to the "tunnel" they opened similarly in another study by Liu et al; they stated that they injected a mixture containing PRP into the femoral head using a method called GDS (Graft Delivery System) (20). Another study reported early results of autologous concentrated mononuclear bone marrow cell injection for non-traumatic osteonecrosis of the femoral head (21). However; there are uncertainties about the injection method in these studies. We believe that the method of application is one of the most important stages in the effectiveness of PRP. The results of our study show that the therapeutic effect of PRP can be increased by improving the application method. In this respect, we wanted to draw attention to an issue that is not sufficiently emphasized in the literature. Our study has unique value in this regard.

Houdek et al. state that the efficacy of PRP applied after core decompression is reduced due to retrograde reflux

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(22). This study emphasizes that the trocar angle is changed and a syringe is used during injection to prevent retrograde reflux. Although this method prevents reflux, we believe that the length of the syringe (Figure 1) is not sufficient for injection with a syringe. In our study, we believe that injection using the length of the K-wire, which is used as a guide for resection, as a reference to solve this problem will increase the effectiveness of the treatment. More work needs to be done on the injection technique and the injection tool used at the method stage. In addition, we believe that an isotonic (2 cc) application (Figure 2) after PRP prevents the recurrence of PRP. Thus, our clinical results support that the effect of PRP increases in the avascular area. Our study highlights the importance of the injection technique and emphasizes that the injection technique is one of the most important stages.

While some studies do not recommend PRP treatment for steroid-induced osteonecrosis, another study emphasizes that it has a place in the treatment of steroid-induced osteonecrosis (15, 22). In our study, we have shown that the use of PRP may have a place in the treatment of cases of avascular necrosis that occur after steroids used in the treatment of Covid-19.

Another study by Aggarwal et al. states that a needle and 3-way cannula is used for PRP application (16). However, the length of the needle and 3-way cannula is not specified in the method section. We believe that needle length is important for PRP efficacy. When the lengths between the spinal needle used in PRP injections and the Nelaton used in our study are evaluated, it is clear that the spinal needle is too short (Figure 1). We have tried to show in our study that the length of the instrument used to reach the necrotic area with PRP is an important step in the treatment of avascular necrosis.

One study highlights that the incidence of hip avascular necrosis may increase in the post-Covid period. This study shows that AVN formation at the femoral head may increase during the COVID-19 epidemic due to high-dose corticosteroid treatment in hospitalized patients (23). Another study highlights cases of avascular necrosis in patients with COVID-19 who did not receive steroid treatment (24). In a meta-analysis of cases of avascular necrosis due to Covid-19 (a systematic review). It states that surgical treatment with core decompression is used in 8.8% of patients with hip avascular necrosis, but does not mention PRP treatment (25). Although there are trials on the use of core decompression for avascular necrosis due to Covid-19, we could not find any trials on the use of PRP for avascular necrosis that develops after Covid-19.

Looking at the literature on the use of PRP after COVID-19 one study on the use of platelet-rich plasma for COVID-19-related olfactory loss emphasizes that olfactory function can be improved to a greater extent with PRP injection after COVID-19 (26). Another study highlights that PRP may be useful in the treatment of hair loss associated with COVID-19 (27).

Another systematic review also found that PRP may be an effective treatment for COVID-19-related olfactory dysfunction. However, it emphasized that more large-scale trials are needed to further investigate the effectiveness of PRP in the treatment of post-COVID-19 olfactory dysfunction (28).

This study is the first in the literature to show that PRP treatment can be added to cord compression for the treatment of patients who develop avascular necrosis after Covid and where PRP is applied using the new technique. However, we believe that further large-scale studies are needed to demonstrate the applicability of PRP and the importance of the method of application in avascular necrosis that develops after Covid-19.

CONCLUSION

Intraoperative local PRP application after core decompression in hip AVN cases is a practice that has a place in the literature, but we believe that there are not enough studies on the importance of the application method. We believe that with the Nelaton catheter application with K-wire guidance performed in our clinic, the local effect of PRP will penetrate better and PRP treatment can be used in avascular necrosis that develops after Covid-19. Our initial results support this idea.

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