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Platelet-Rich Plasma Enhanced Bone Autograft in Femoral Head Necrosis-A Case Series Report on a Six-Year Follow-Up Period

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Abstract

Aim: We compared the long-term results of two treatment regimes in avascular femoral head necrosis.

Methods: We performed a retrospective clinical observational study on 19 hips that were operated on by core decompression and autologous bone impaction enhanced with platelet-rich plasma (platelet-rich plasma+bone autograft group). As a control, 13 hips were operated on by core decompression only (decompression group). Joint replacement was evaluated as the primary endpoint of the study, functional results were evaluated according to the Harris Hip Score and bone density measurements were performed.

Results: Prosthesis implantation was significantly less frequent in the platelet-rich plasma+bone autograft group than in the decompression group ($p<0.05$). In the platelet-rich plasma+bone autograft group, operated hip function at follow-up declined according to advancement of the preoperative Ficat stages. No specific pattern in the bone density scoring was identified between the groups analyzed.

Conclusion: The combination of platelet-rich plasma with core decompression and autologous bone impaction may be an effective method in lowering the need for hip prosthesis implantation in the treatment of femoral head avascular necrosis.

Keywords: Platelet-rich plasma; Femoral head avascular necrosis; Bone regeneration; Growth factor

Abbreviations AVN: Avascular Necrosis; MRI: Magnetic Resonance Imaging; PRP: Platelet-rich Plasma; ROI: Regions of Interest; THR: Total Hip Replacement

Introduction

The incidence rate of avascular necrosis (AVN) in the femoral head is continuously increasing among the young adult population [1,2]. Without specific and efficient treatment, the disease progresses in 84% of cases to the need for total hip replacement (THR) of the collapsed femoral head [3]. Numerous treatment options have been suggested, e.g. physiotherapy, core decompression, osteotomies, vascularized bone grafting, free fibular transfer, etc., however, none of them have represented a breakthrough [4-7]. The gold standard procedure in most countries is core decompression, during which one or more holes are drilled into the femoral head from a retrograde direction [8]. A similar therapeutic protocol is applied in other types of osteonecrosis or osteochondral lesions [9-13]. The exact mode of action is unknown and even the terminology is misleading, since the bone oedema in the affected area may not actually contribute to higher hydrostatic pressure. However, drilling or microfracture likely causes a controlled injury of the bone without affecting the overall structure or stability. The injury-induced bone remodelling process can lead to superior tissue quality compared to the original material. According to studies with long-term follow-up, the failure rate of this procedure is between 15-71% [14]. Theoretically, the regenerative process induced by the limited injury of drilling can be further supported by the application of bone autografts and growth factors [15].

Bone autografts from freshly harvested morsellized chips are commonly used for bone substitution, with those from the iliac crest believed to be the best available bone graft. However, since the bone autograft is implanted into a tissue space that has impaired viability, it is reasonable to induce bone remodelling by adding growth factors to the graft. One line of research using bone extracts such as demineralized bone matrix led to the development of injectable bone morphogenic proteins [16-18]. Other investigations were based on the principle of blood-derived factors such as platelet-rich plasma (PRP) [19,20]. While cancellous bone augmentation with PRP in the maxillo-facial area is supported by the majority of the earlier studies, its effect is still somewhat controversial [21]. Moreover, the evidence for using PRP in the treatment of AVN is limited. For instance, Pak et al. used PRP together with adipose-derived stem cells in the case of two patients and reported promising results [22,23]. In another study, the technical details of the use of PRP alone and the mixture of PRP and bone graft through an arthroscopic approach were also described with promising outcomes in a short-term follow-up period [24]. Due to the

small number of patients in each group, it is difficult to draw any definitive conclusions from this study. There are more clinical data using a treatment protocol by which PRP is applied as an adjuvant to bone marrow derived cell implantation. Martin and colleagues presented a case series of 77 hips treated with this technique which resulted in a 79% hip retention rate in 1.5 years mean follow-up [20]. Similar short-term results were reported by Gangji et al. [25]; however, there was a progression of the disease until the second, 5 years follow-up period [26]. This study highlighted that although short-term results can be achieved with several methods, further therapeutic approaches are needed that can promise meaningful regeneration of the femoral head structure. In the current study, we investigated the 6 years therapeutic effect of PRP mixed with bone autografts in a series of clinical cases of avascular femoral head necrosis.

Materials and Methods

Patients

All investigations were carried out under the guidelines of the Ethical Committee of the Polyclinic of the Hospitaller Brothers of St. John of God and Semmelweis University, Department of Orthopedics. Written patient consent was obtained from all participants in the investigational group. During the time frame of January 1, 2003 to January 6, 2006, 32 hips in 31 patients were operated due to femoral head necrosis (AVN) by either the classical core decompression technique described by Ficat (decompression group) or by decompression enhenced with bone+PRP autografting (PRP+bone autograft group) [27]. The two treatment groups were based on the patients of two main orthopaedic centers that were using different treatment strategies in cases of femoral head AVN: one center used the classical core decompression technique; the other center used core decompression enhanced with bone+PRP autografting. In the decompression group (n=13), the lateral trochanteric approach was used, and core decompression was performed under fluoroscopic guidance. In 9 of the cases, a 6.5 mm drill bit was used, and in 4 of the cases, multiple small-diameter drilling was performed using a 3.2 mm drill bit. The operations in the decompression drilling group were carried out by 9 surgeons, all working under the same general protocols, however, the choice of single or multiple drilling was decided by surgeon's preference. In the PRP+bone autograft group (n=19) all the operations were carried out by two of the authors (TL and BM). The cortex at the border between the femoral head and neck was exposed and trephinated through an antero-lateral approach (Watson-Jones), and cancellous bone harvested from the iliac crest through a second incision was manually mixed with the activated PRP and impacted into the bone cavity. The majority of the patients had idiopathic AVN with no known etiology, 3 patients had ulcerative colitis and 1 had posttraumatic osteonecrosis. The male/female ratio of the patients was significantly higher in the PRP+bone autograft group versus the decompression group, however, neither of them was different from the expected 3/1 to 8/1 ratio described in the AVN epidemiology literature [28]. The key patient characteristics are summarized in Table 1.

PRP preparation

Autologous blood (60 ml) was drawn through an iv. catheter before starting the surgical procedure and before administration of any fluids. PRP was prepared on the day of the operation using the SmartPreP® 2 system (Harvest Technologies, Plymouth, MA) according to the manufacturer's instructions. The PRP was activated by autologous thrombin prepared with the SmartPreP® 2 system.

	Control	PRP+autograft
Number of operated patients/ hips	13/13	18/19
Number of evaluated patients/ hips	12-Dec	16/17
Mean age (years)	46.3 ± 12.8	45.3 ± 12.6
Mean follow-up time (years)	5.9 ± 0.8	6.1 ± 1.1
Male: Female ratio	6:06	16:01
Preop. Ficat stage (I:II:III)	5:07:00	2:10:05
Etiology	32 – no known etiology	
	3 – ulcerative colitis	
	1 – posttraumatic osteonecrosis	

Table 1: The primary characteristics of patients. Only the male/female ratios was significantly different between the two groups, however, neither one was significantly different from the historical 3/1 to 8/1 male/female ratio.

Follow-up

Two patients in the PRP+bone autograft group died due to unrelated causes, and one patient was lost to follow-up in the decompression drilling group. One patient was operated on both sides in the PRP+bone autograft group, so altogether there were 12 patients in the decompression group and 17 hips in 16 patients in the PRP +bone autograft group who were evaluated in the study. Joint replacement of the affected hip was evaluated as a primary end point of the study. The mean follow-up time was 6.07 ± 1.11 years in the PRP +bone autograft group and 5.9 ± 0.76 years in the decompression group. During the follow-up visits, x-ray, magnetic resonance imaging (MRI) and bone density (DXA) scans were performed in order to follow the progression/regression of the disease in cases without prosthesis implantation. MRI scans were done in the same center pre- and post-operatively using identical settings. Pre- and post-operative Ficat stages for both groups were blindly evaluated by 3 independent orthopedic surgeons. Hip functions were blindly evaluated according to the Harris Hip Score system by an independent investigator. Regions of interest (ROIs) on the DXA images were selected as a large circle area to cover the femoral head and 5 other small circles of equal size in the four quadrants and the middle.

Statistical analysis

Results are reported as mean ± SEM or numerical values. Statistical significance between two measurements was determined by two-way ANOVA and Newman-Keuls post-hoc tests or Fisher's exact test for postoperative FICAT observations and t-test for Harris Hip Score. Probability values of $p<0.05$ were considered significant.

Results

Preoperative Ficat classification of the patients was comparable in both groups, mostly Ficat stage II at the time of operation (58% of the

PRP+bone autograft and 62% of the decompression group). The primary endpoint of the study was hip prosthesis implantation during the follow-up, which was performed in 4 cases (24%) in the PRP+bone autograft group and 8 cases (67%) in the decompression group ($p<0.05$). In cases where the joint was still preserved at the time of follow-up, a general deterioration of the Ficat staging was observed (Figure 1). Although the small number of patients living without hip prosthesis after the core decompression does not allow any statistical evaluation, the remaining joint functions were comparable between the two groups (Harris Hip Score PRP+bone autograft vs. decompression: 81.3 ± 4.9 vs. 85.4 ± 10.1). This observation was further supported by the MRI exams, which did not show any differences that would justify changes in the Ficat scoring. Evaluating bone mineral density of the six ROIs of the affected femoral heads showed a clear difference among the left and the right side of the patients when both joints were available (ROI 1-6 affected side vs. unaffected side: 1.88 vs. 1.59; 2.67 vs. 2.19, 1.73 vs. 1.37; 1.86 vs. 1.67; 1.41 vs. 1.22; 2.14 vs. 1.87 [g/cm^2]) , however, there was no difference among the treatment groups (ROI 1-6 PRP+bone autograft group vs. decompression: 2.01 vs. 1.84; 2.68 vs. 2.68; 2.01 vs. 1.64; 1.94 vs. 1.83; 1.55 vs. 1.23; 2.3 vs. 1.92 [g/cm^2]). Again, due to the low number of surviving joints in the decompression group, this data can only be treated as descriptive.

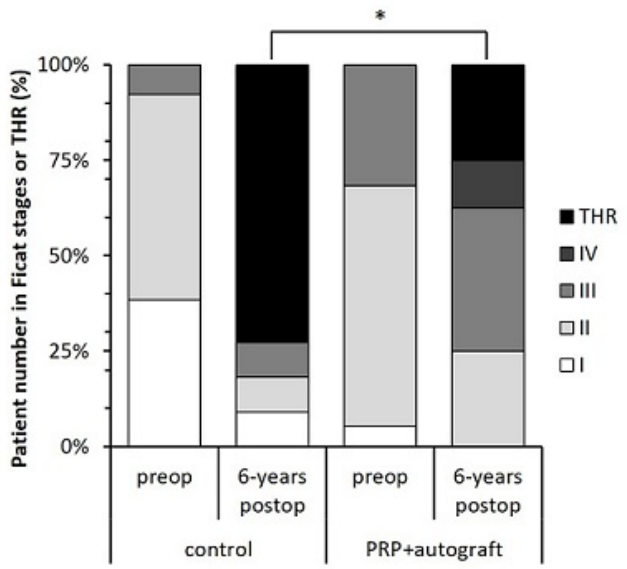

Figure 1: Patient number in Ficat stages or THR (%). Prosthesis implantation was significantly less frequent in the platelet-rich plasma+bone autograft group than in the decompression drilling group ($p<0.05$).

Discussion

In the present study we found a significantly better outcome for AVN in cases where the femoral head was impacted with a mixture of autograft and PRP compared to the core decompression therapy. The long-term follow-up of 6 years and the highly relevant endpoint of joint survival in the present study add significant support to the pilot findings that PRP-enhanced grafting can have a beneficial effect on the progress of AVN. The general conclusion among orthopedic surgeons is that treatment of AVN is successful in about 70-80% of the cases regardless of which method is applied. Due to the fact that the core decompression technique is minimally invasive and easy to perform, this became the gold standard of care. In a critical review of the literature, Marker and colleagues compared the outcome data from several clinical investigations, and concluded that pre-1992 studies reported somewhat worse outcomes than those published between 1992 and 2007 [14]. In earlier studies performing additional surgery as outcome criteria, with 5 year follow-up, the failure rate ranged between 19% and 71% with a median of 50%. Even in the later studies, using presumably improved tools and better aftercare, the failure rate still ranged between 3% and 58%, with a median of 35%. The data from our current treatment groups fall within this range, close to the ends of the spectrum. The very high variation in the reported success rate in some studies is probably due to the high variation of follow-up times. For example, it is difficult to interpret a data set for a 1-176 month follow-up period [29].

Therefore, in the present study, we aimed to obtain a uniform follow-up time of 70 months, which allowed a more meaningful comparison between the two treatment protocols: one was decompression drilling performed in slightly different ways by a group of surgeons, representing the 'standard of care', and the other was an investigational protocol carried out by one separate team with a promising, but more invasive and costly procedure. Although the male/female ratio of the two treatment groups differed, these were close to the expected ranges described in the literature [30]. As gender is not a factor that affects the progression of the disease, we believe that this difference did not introduce significant bias into our observations [31]. One limitation of the current study is the lack of two treatment groups, namely autograft only and PRP only. Although the inclusion of these groups would be obvious in case of an animal experiment, it is ethically challenging in the case of a human study even if it limits the interpretation of the results. Patients who agreed to undergo a procedure (even if since the minimal invasive method was developed for the PRP+bone autograft method also), justifiably wanted the full feature set (in our case bone autograft and PRP implantation) and not just either PRP or allograft only. Although neither the PRP only nor the autograft only procedure is unethical, in the case of a perceived complete treatment option, it is only ethical to offer this to the patients. Thus, it was not possible for us to evaluate the individual contributions of PRP or autograft to the overall effect. Moreover, recent studies add a further layer of complexity to the procedure by stem cell implantation in AVN, which was not considered in the current study, but may be introduced later in order to move towards a complete biological regeneration of the femoral head [31,32].

Conclusion

We hereby conclude that the combination of PRP with core decompression and autologous bone impactation may be an effective method in the treatment of avascular necrosis of the femoral head. Based on these encouraging results, the initiation of additional prospective studies may support the overall long-term efficacy of such treatment regimes.

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Author Contributions

All authors make substantial contributions to conception and design, and interpretation of data. Tamás Lakatos and Bálint Major contributed equally in the present study with study design and performing operations. Péter Somogyi and Gabriella Vácz: acquisition and analysis of clinical data, Simon Melinda and István Hornyák: writing manuscript, Zsombor Lacza: statistical analysis, writing manuscript. Authors had read and approved the final manuscript.

Competing Interests

The authors declare no conflict of interest.

References

1. Mont MA, Zywiel MG, Marker DR, McGrath MS, Delanois RE (2010) The natural history of untreated asymptomatic osteonecrosis of the femoral head: A systematic literature review. J Bone Joint Surg Am 92: 2165-2170.
2. Hernigou P, Habibi A, Bachir D, Galacteros F (2006) The natural history of asymptomatic osteonecrosis of the femoral head in adults with sickle cell disease. J Bone Joint Surg Am 88: 2565-2572.
3. Saito S, Ohzono K, Ono K (1988) Joint-preserving operations for idiopathic avascular necrosis of the femoral head. Results of core decompression, grafting and osteotomy. J Bone Joint Surg Br 70: 78-84.
4. Malizos KN, Karantanas AH, Varitimidis SE, Dailiana ZH, Bargiotas K, et al. (2007) Osteonecrosis of the femoral head: etiology, imaging and treatment. Eur J Radiol 63: 16-28.
5. Babis GC, Sakellariou V, Parvizi J, Soucacos P (2011) Osteonecrosis of the femoral head. Orthopedics 34: 39.
6. Camporesi EM, Vezzani G, Bosco G, Mangar D, Bernasek TL (2010) Hyperbaric oxygen therapy in femoral head necrosis. J Arthroplasty 25: 118-123.
7. Agarwala S, Shah SB (2010) Ten-year follow-up of avascular necrosis of femoral head treated with alendronate for 3 years. J Arthroplasty 26: 1128-1134.
8. Lavernia CJ, Sierra RJ (2000) Core decompression in atraumatic osteonecrosis of the hip. J Arthroplasty 15: 171-178.
9. Harreld KL, Marulanda GA, Ulrich SD, Marker DR, Seyler TM, et al. (2009) Small-diameter percutaneous decompression for osteonecrosis of the shoulder. Am J Orthop (Belle Mead NJ) 38: 348-354.
10. Stroh DA, LaPorte DM, Marker DA, Johnson AJ, Mont MA (2012) Atraumatic osteonecrosis of the distal radius and ulna: case series and review. J Hand Surg Am 37: 134-141.
11. Marulanda GA, McGrath MS, Ulrich SD, Seyler TM, Delanois RE, et al. (2010) Percutaneous drilling for the treatment of atraumatic osteonecrosis of the ankle. J Foot Ankle Surg 49: 20-24.
12. Imade S, Kumahashi N, Kuwata S, Kadowaki M, Tanaka T, et al. (2012) A comparison of patient-reported outcomes and arthroscopic findings between drilling and autologous osteochondral grafting for the treatment of articular cartilage defects combined with anterior cruciate ligament injury. Knee 20: 354-359.
13. Kim YS, Park EH, Lee HJ, Koh YG, Lee JW (2012) Clinical comparison of the osteochondral autograft transfer system and subchondral drilling in osteochondral defects of the first metatarsal head. Am J Sports Med 40: 1824-1833.
14. Marker DR, Seyler TM, Ulrich SD, Srivastava S, Mont MA (2008) Do modern techniques improve core decompression outcomes for hip osteonecrosis? Clin Orthop Relat Res 466: 1093-1103.
15. Nauth A, Ristevski B, Li R, Schemitsch EH (2011) Growth factors and bone regeneration: how much bone can we expect? Injury 42: 574-579.
16. Geesink RGT, Hoefnagels NHM, Bulstra SK (1999) Osteogenic activity of OP-1 bone morphogenetic protein (BMP-7) in a human fibular defect. J Bone Joint Surg Am 81-B: 710-718.
17. Wang EA, Rosen V, Cordes P, Hewick RM, Kriz MJ, et al. (1988) Purification and characterization of other distinct bone-inducing factors. Proc Natl Acad Sci U S A 85: 9484-9488.
18. Howell TH, Fiorellini J, Jones A, Alder M, Nummikoski P, et al. (1997) A feasibility study evaluating rhBMP-2/absorbable collagen sponge device for local alveolar ridge preservation or augmentation. Int J Periodontics Restorative Dent 17: 124-139.
19. Wroblewski AP, Mejia HA, Wright VJ (2010) Application of platelet-rich plasma to enhance tissue repair. Operative Techniques in Orthopaedics 20: 98-105.
20. Martin JR, Houdek MT, Sierra RJ (2013) Use of concentrated bone marrow aspirate and platelet rich plasma during minimally invasive decompression of the femoral head in the treatment of osteonecrosis. Croat Med J 54: 219-224.
21. Kotsovilis S, Markou N, Pepelassi E, Nikolidakis D (2010) The adjunctive use of platelet-rich plasma in the therapy of periodontal intraosseous defects: a systematic review. J Periodontal Res 45: 428-443.
22. Pak J (2011) Regeneration of human bones in hip osteonecrosis and human cartilage in knee osteoarthritis with autologous adipose-tissue-derived stem cells: a case series. J Med Case Rep 5: 296.
23. Pak J (2012) Autologous adipose tissue-derived stem cells induce persistent bone-like tissue in osteonecrotic femoral heads. Pain Physician 15: 75-85.
24. Guadilla J, Fiz N, Andia I, Sanchez M (2012) Arthroscopic management and platelet-rich plasma therapy for avascular necrosis of the hip. Knee Surg Sports Traumatol Arthrosc 20: 393-398.
25. Gangji V, Hauzeur JP, Matos C, De Maertelaer V, Toungouz M, et al. (2004) Treatment of osteonecrosis of the femoral head with implantation of autologous bone-marrow cells. A pilot study. J Bone Joint Surg Am 86A: 1153-1160.
26. Gangji V, De Maertelaer V, Hauzeur JP (2011) Autologous bone marrow cell implantation in the treatment of non-traumatic osteonecrosis of the femoral head: Five year follow-up of a prospective controlled study. Bone 49: 1005-1009.
27. Ficat RP (1985) Idiopathic bone necrosis of the femoral head. Early diagnosis and treatment. J Bone Joint Surg Br 67: 3-9.
28. Kamal D, Alexandru DO, Kamal CK, Streba CT, Grecu D, et al. (2012) Macroscopic and microscopic findings in avascular necrosis of the femoral head. Rom J Morphol Embryo 53: 557-561.
29. Bellot F, Havet E, Gabrion A, Meunier W, Mertl P, et al. (2005) Core decompression of the femoral head for avascular necrosis. Rev Chir Orthop Reparatrice Appar Mot 91: 114-123.
30. Diana Kamal RT, Alexandru DO, Grecu DC, Mogoanta L (2013) Epidemiologic Study of Avascular Necrosis of the Femoral Head. Curr Health Sci J 39: 6.
31. Houdek MT, Wyles CC, Martin JR, Sierra RJ (2014) Stem cell treatment for avascular necrosis of the femoral head: current perspectives. Stem Cells Cloning 7: 65-70.
32. Aarvold A, Smith JO, Tayton ER, Jones AM, Dawson JI, et al. (2013) A tissue engineering strategy for the treatment of avascular necrosis of the femoral head. Surgeon 11: 319-325.