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A study on bone marrow derived stem cells and its application on ACL graft regeneration in partial ACL tears

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Abstract
Background: Partial tears of the anterior cruciate ligament (ACL) are frequent, and there is still considerable controversy surrounding their diagnosis, natural history and treatment.
Aim: To examine patient-reported outcomes, physical examination and magnetic resonance imaging (MRI) findings of partial ACL tears treated with an intraarticular injection of BMAC and to evaluate both subjective and objective clinical results as to compare the outcomes Pre Procedure, at 3 weeks and 3 months following the procedure, as well as functional recovery time.
Methods: From April to July 2023, consecutive patients from a single institution with partial ACL tears treated nonoperatively were prospectively evaluated. Partial tears were defined as a positive Lachman test with clear endpoint, a negative pivot-shift and MRI were taken and were classified and graded on the basis of VAN MEER Radiological Classification. Patients were treated with one intraarticular injection of BMAC and specific physical therapy protocol. Prospective analyzed data included physical examination and Lysholm and International Knee Documentation Committee scores were taken Pre Procedure, at 3 weeks and 3 months. Baseline MRI findings and at 3 months follow-up were reviewed. Failure was defined as those patients with clinical instability at follow-up that required ACL reconstruction at 3 months.
Results: A total of 30 patients where included, all 30 treated with BMAC injection with a mean follow-up of 3 months. Their Mean Age was 40. 20 (60%) of them were men and 40 % of them were females, Overall failure rate was (n = 3). One patient (5.0%) was unable to RTS due to subjective instability. The other 95.0% in each group were able to return to their previous sports level. Regarding objective stability, at 6 month follow-up in group 1, 19 presented a decrease in the side-to-side difference, 10 remained with the same difference, and 1 had 2 mm more, over all, mean RTS time was 3 months. Significant differences were observed regarding subjective outcomes, return to sport Following Procedure. MRI findings revealed an improvement in the ACL signal in half of the patients. However, we did not find a significant relationship between MRI findings and clinical outcomes.
Conclusion: Overall, 95.0% of patients returned to sports at a mean follow-up of 3 mo. Mean time to return to sports was 3 months. The addition of BMAC shows promise in the treatment of grade 1, 2, and possibly grade 3 ACL tears without retraction. Further investigation using a controlled study design is warranted.

Keywords: ACL Tears, BMAC injection, minimally invasive surgical procedure, Partial ACL Tear.

Introduction
Partial tears of the anterior cruciate ligament (ACL) account for approximately 10% to 30% of all ACL tears [1, 2]. ACL tears can be complete, leading to long-term instability in a substantial percentage of patients, or partial, with an uncertain natural history [3-10]. The diagnosis, natural history, and treatment of this type of injury remain highly debated [11-13]. Conservative management may yield favorable outcomes for partial ACL tears if sports activity is limited, while surgical indications are present for both partial and complete ruptures with continued instability or ligament injury during pivoting sports [14-16] Diverse criteria are used to define partial ACL tears, including MRI assessments of the extent of torn fibers, affected bundle (anteromedial or posterolateral), and tear location (proximal, middle third, or distal). Physical examination plays a crucial role in identifying these injuries [17].

Arthroscopy is considered the gold standard for diagnosing the macroscopic integrity of the intact bundle, confirmed by finding intact remnant ACL fibers from femur to tibia insertion points [18-20]. Although ACL reconstruction can have good success rates, it may not fully restore physiological movement due to the graft's biomechanically disadvantageous location, leading to increased tibial rotation and impaired neuromuscular control [21]. Unlike complete ACL tears, which have limited intrinsic healing capacity, the potential for healing in partial ACL tears has been a topic of discussion. Alternative treatments are being explored to preserve ligament integrity and knee joint biomechanics, Favorable outcomes have been reported with nonoperative or surgical treatments (such as repair or augmentation) and various biological approaches. However, conservative treatment has been associated with progression to complete ACL deficiency and symptomatic knee laxity in some cases [22-24]. These therapies aim to promote healing, preserve proprioceptive nerve fibers, collagenous architecture, and normal knee joint biomechanics [25] In recent years, Bone Marrow Aspiration Cytology (BMAC) injections have gained significant attention as a biologic treatment for sports-related injuries. BMAC contains growth factors and bioactive proteins that can enhance tis sue healing [11-14]. BMAC is used in ligament injuries, including the ACL, has been on the rise, mostly focusing on biologic augmentation for graft healing after ACL reconstruction. However, only a limited number of studies have specifically investigated using BMAC AND PRP to promote healing of native injured ACL [26]. Several experimental techniques using extracellular matrix, PRP, or bone marrow-derived MSCs have shown promise in promoting healing and improved function in animal models [27], In situ repair of ACL tears with MSCs may have benefits in maintaining normal biomechanics, aiding cartilage repair, and preserving proprioception [28]. The purpose of this study is to evaluate patient-reported outcomes, physical examination findings, and MRI results in partial ACL tears treated with intraarticular BMAC injection and evaluate their results pre procedure, at 30 mins post procedure, 3 weeks post procedure and 3 months post procedure. It focuses on treating MRI-documented ACL tears in adults using bone marrow concentrate rich in MSCs. The efficacy of this regenerative therapy is assessed through pain and functional outcome measures, along with MRI evidence of structural changes in the ACL [29]. Aims to explore the safety and preliminary efficacy of this treatment for different ACL injuries, potentially benefiting patients who may not be suitable for surgery or wish to avoid it [30]. By understanding the outcomes of this treatment, it lays the groundwork for future rigorous investigations in the field.

Methodology and Research Design

A prospective study was be conducted among 30 patients presenting to an interventional pain practice with complaints of knee instability with or without pain and with an ACL tear previously documented with MRI, and laxity with Lachman testing on exam were enrolled in a case series of the first set of ACL treatments. Patients were not paid for their participation. Patients were included in the analysis of prospectively collected data if they had a grade 1, 2, or 3 ACL tear without greater than 1 cm retraction. We defined retraction as any visible area of increased MRI signal intensity within the substance of the ligament that was full thickness and resulted in a discontinuity of the course of the structure. To my knowledge, this is the first study of ACL tears to focus on the extent of the separation of torn ACL fragments, thus this delineation has not been validated previously. Patients who presented during the period between August 2022 and March 2023 were studied. Patients who were treated during acute (1 month postinjury), subacute injury (1-6 months postinjury), or in a chronic state of injury (6 months postinjury) 18 were eligible for inclusion. Exclusion criteria were grade 3 ACL tear with 1 cm retraction, active neoplasm within the past 5 years, a history or presence of anemia, or age younger than 16 years. Patients provided consent verbally and in writing. Clinical outcomes for pain and function were recorded at baseline and prospectively at 1 month, 3 months, 6 months, and annually following treatment. Additionally, percentage improvement on a Likert scale was recorded at 1 month, 3 months, 6 months, and annually following treatment. Institutional review board approval was provided by the college. ACL injuries were graded as follows:

Grade 1 sprain: The ligament is partial torn, with less than half of the ligament substance disrupted.

Grade 2 sprain: The ligament is partially torn, with more than half of the ligament substance disrupted.

Grade 3 sprain: The ligament is completely torn.

The Treatment protocol consisted of Preinjection which was the first step consisting of a hypertonic dextrose solution into the ACL 2–5 days prior to injection of the BMC. The purpose of this preinjection procedure was to introduce a chemical irritant to the ACL in order to prompt a brief inflammatory response. A 25-gauge 3.0 inch needle was inserted through the skin overlying the patellar tendon and directed through the inferior patellar tendon to a location just anterior to the tibial spine, on lateral fluoroscopy. Midline needle placement was confirmed on the anterior posterior fluoroscopic view. Iodixanol radiographic contrast was injected to confirm flow in the ACL sheath traveling between the radiographic origin and insertion landmarks, in both views. This was followed by injection of 3-5 mL of 12.5% dextrose and 0.1% lidocaine in normal saline. Harvest and concentration of bone marrow aspirate the next step of the treatment was to harvest bone marrow and isolate the portion containing MSCs from each patient, in preparation for reinjection. Prior to the procedure, the patients were restricted from taking corticosteroids and nonsteroidal anti-inflammatory drugs (NSAIDs) for at least 2 weeks, as these medications can impair soft tissue healing.

Results

In our study, A total of 30 patients where included. In total, all 30 were treated with Bone Marrow Derived Stem cell injection with a mean follow-up of 3 months had their symptoms improve gradually over 3 months as measured by IKDC Scoring and van meer Radiological Scoring and Return to Activities at 3 months. The mean age was 41, 18 of them were males and 12 of them were females,15 of them were involving the right knee and the rest 15 involving the left knee. Three were degenerative type of tears and remaining 27 were traumatic, 18 of them were grade 2 acl injury whereas 12 of them were grade 1, total number of proximal tears involved were 16 and total number of midsubstance tears involved were 15 [Table 1]. The patients were monitored for a total of three months during which time their symptoms gradually got better. With the exception of one patients, whose IKDC Score was 44 (before injection), 46 (3 weeks post injection) and 49 at 3 months (post injection). Mean IKDC Scoring pre procedure was 45.Mean IKDC Scoring 3

weeks post procedure was 56.Mean IKDC 3 months post procedure was 72, [Table 2], [Figure 1 and Figure 2] van meer Radiological Scoring had improved for everyone at the end of 3 months except for one case in which it did not change pre injection and post injection, Among all the others it had improved at three months by a score of 1 or more than 1.Mean Van Meer Score Pre procedure was 6.5 and 3 months post procedure was 4.6 [Table 3], [Figure 3]. In Majority of the patients (29 of them) had returned to activities after 3 months except for one. It demonstrated that the progressive improvement observed persisted throughout the follow-up period of 3 months. There were no complications seen in any of the patients and patients were able to do all their daily activities without the use of pain medication.

Discussion

Partial tears of the anterior cruciate ligament (ACL) comprise approximately 10% to 30% of all ACL tears [31-34]. The accurate diagnosis of such tears remains challenging, leading to some cases going undetected. Relying solely on physical examination is not sufficient to distinguish between partial ACL tears and intact ACLs [37]. Similarly, MRI, while helpful, exhibits limited accuracy (ranging from 25.0% to 50.0%) in diagnosing partial ACL tears due to overlapping imaging findings with complete tears and other factors [38].

As a result, arthroscopy is often used by surgeons to assess the extent of the injury. A recent study investigated the correlation between preoperative clinical assessment and arthroscopic examination in patients with ACL tears [39]. Evaluation under anesthesia demonstrated high sensitivity (100%) in detecting partial tears but lacked specificity (65.5%), leading to a significant number of false-positive diagnoses. Conversely, MRI showed relatively high sensitivity (90.9%) and specificity (85.7%), with an overall accuracy of 86.3%, surpassing that of evaluation under anesthesia (69.5%) [40].

Regarding nonsurgical management for partial ACL tears, a systematic review by Pujol *et al.* [8] analyzed 12 articles confirming the diagnosis through arthroscopy without ACL surgery. Patients were followed for an average of 5.2 years (ranging from 1.0 to 15.0 years), with favorable short- and mid-term functional outcomes observed, particularly when sports activities were restricted. The mean rate of revision ACL surgeries was 8.1% (ranging from 0% to 21.0%), and the return-to-sport (RTS) rate was 52.0% (ranging from 21.0% to 60.0%). In contrast, Noyes *et al.* [7] reported a progression to complete ACL rupture in 38.0% of cases in their prospective evaluation of 32 patients with partial ACL tears. Lehnert *et al.* [28] found that 56.0% of 39 partial ACL tear patients had progressed to ACL deficiency five years after the initial injury. Fritschy *et al.* [9] reported a 42.0% rate in 43 patients, while Fruensgaard *et al.* [29] reported 51.0% in a series of 41 patients. Our overall failure rate was 10.0%, with 90.0% of patients returning to the same level of sports participation, though it is essential to consider historical context and indications for ACL surgery used three decades ago. Notably, some patients displayed significant side-to-side differences in KT-1000 arthrometric evaluation, suggesting potential lack of healing of ACL fibers, especially when the anteromedial bundle was affected, despite remaining active in their sports participation.

In current research on ACL repair and healing, the use of biologic agents such as growth factors, platelet-rich plasma (PRP), stem cells, and biological scaffolds has gained attention [41]. Most studies (21 out of 23) have focused on applying biologic agents during ACL reconstructive surgery, while only two case series have explored their potential in treating partial ACL tears [42, 43]. Centeno *et al.* [30] conducted a prospective case series involving 10 patients who underwent percutaneous injection of autologous bone marrow nucleated cells, guided by fluoroscopy. At a mean follow-up of 3 months, seven out of ten patients showed improvements in MRI measures of ACL integrity. However, this study lacked a control group and involved multiple components in the treatment protocol. Conversely, Seijas *et al.* [20] presented a retrospective case series of 19 football players with partial ACL tears treated with arthroscopic intraligamentary application of PRP (leukocyte-poor). All cases involved a complete rupture of the anteromedial bundle with an intact posterolateral bundle, and the RTS rate was 84%. In our study the RTS Rate was 90%. We admit that this study has several limitations, Three Months following the procedure we are reporting the interim results, our sample size was small and the time frame of this study was short. Our study lacks a control group. However, the addition of BMAC shows promise in the treatment of grade 1, 2, ACL tears. Further investigation using a controlled study design is warranted.

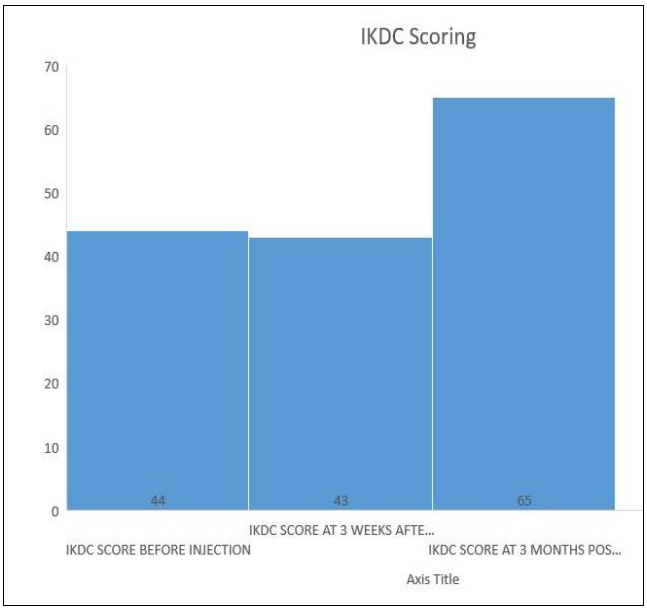

Fig 1: IKDC Scoring Comparison

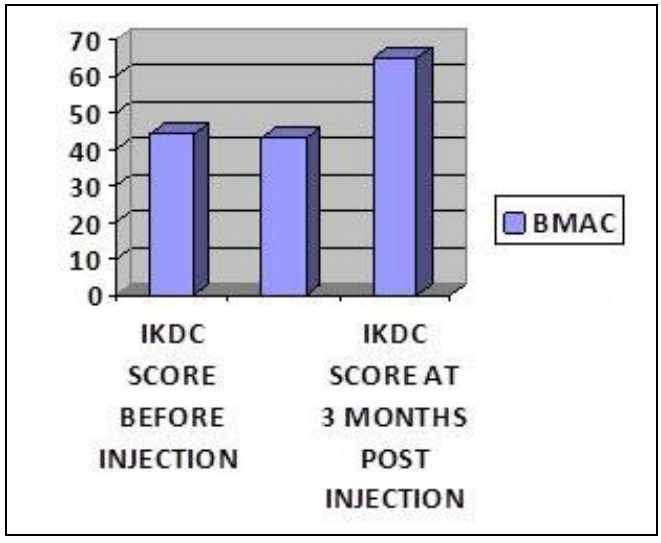

Fig 2: IKDC Scoring Comparison

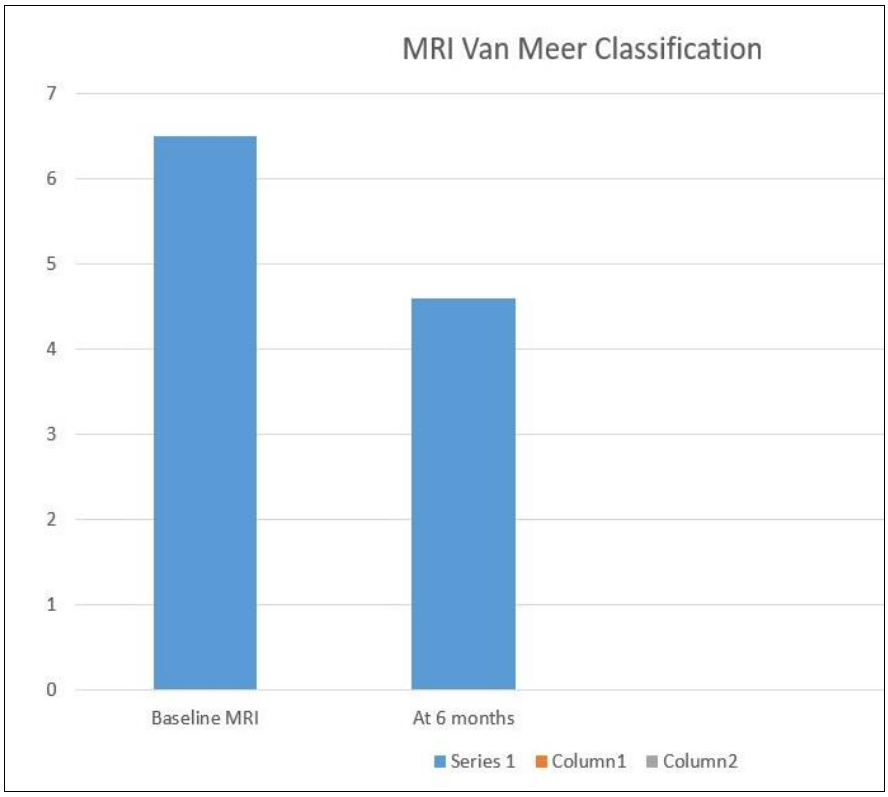

Fig 3: MRI Van Meer Scoring

Table 1: Demographic Data

N-30	
Age in Year Median	**41 Years**
Males	18
Females	12
Degenerative Tears	3
Traumatic Tears	27
MRI tear location	
Proximal, n (%)	16
Mid-substance, n (%)	15
Grade 1 injury	12
Grade 2 injury	18

Table 2: Results at final follow-up

Baseline	**N-30**
Lysholm score, (IQR)	
IKDC score, mean (IQR)	45
IKDC Score 3 weeks, Mean	56
At final follow-up	7
Lysholm score, median (IQR)	
IKDC score, median (IQR)	
TAL, mean ± SD	
RTS rate, n (%)	
Time to RTS in mo, mean ± SD	
Failure rate, n (%)	

Table 3: Magnetic resonance image Van Meer classification at baseline and at 6 m

MRI Van Meer classification	N-30
Baseline MRI, mean PRE Procedure	6.5
MRI at 6 months follow-up, mean	4.6

Table 4: Patient demographics and data

Sr. No	Age	Sex	Side	Etiology	ACL Tear Grading	MRI Tear	Treatment Given	IKDC Score Before Injection	IKDC Score at 3 weeks after injection	IKDC score at 3 months post injection	Return to activities at 3 weeks	Return to activity at 3 m	Van meer classification score pre injection	Van meer radiological classification score at 3 m post injection
1	35	M	L	Trauma	2	Proximal	BMAC	44	43	65	√		6	4
2	24	M	R	Trauma	2	Midsubstance	BMAC	33	38	76	√		7	5
3	45	M	L	Trauma	1	Proximal	BMAC	37	44	67		√	7	6
4	53	F	R	Trauma	1	Midsubstance	BMAC	45	49	62		√	6	5
5	49	F	R	Trauma	2	Midsubstance	BMAC	43	54	68	√		5	4
6	63	M	L	Degen	2	Proximal	BMAC	46	56	65		√	6	4
7	58	M	R	Trauma	2	Proximal	BMAC	42	45	48			7	7
8	34	M	L	Trauma	1	Proximal	BMAC	39	56	67	√		7	2
9	39	M	L	Trauma	1	Midsubstance	BMAC	45	57	78	√		6	4
10	28	M	R	Trauma	2	Midsubstance	BMAC	54	68	79	√		7	3
11	20	F	R	Trauma	1	Proximal	BMAC	42	56	76	√		7	5
12	47	M	L	Trauma	1	Midsubstance	BMAC	46	59	79	√		6	6
13	26	F	R	Trauma	2	Midsubstance	BMAC	42	56	66	√		6	4
14	37	F	L	Trauma	1	Proximal	BMAC	53	67	78	√		7	5
15	42	F	L	Degen	2	Midsubstance	BMAC	48	54	77		√	6	5
16	35	M	R	Trauma	2	Proximal	BMAC	53	65	72	√		7	5
17	48	M	R	Trauma	1	Midsubstance	BMAC	38	54	80		√	6	4
18	40	M	R	Trauma	2	Midsubstance	BMAC	56	64	82	√		7	5
19	24	M	R	Trauma	2	Proximal	BMAC	42	56	75	√		6	3
20	26	F	L	Trauma	2	Midsubstance	BMAC	45	60	74	√		6	4
21	33	M	L	Trauma	1	Midsubstance	BMAC	41	45	67	√		5	3
22	29	F	R	Trauma	2	Proximal	BMAC	48	57	84	√		7	5
23	22	M	L	Trauma	2	Midsubstance	BMAC	47	58	59	√		8	8
24	57	M	L	Degen	1	Proximal	BMAC	44	46	53	√		7	7
25	36	F	R	Trauma	1	Midsubstance	BMAC	46	57	75		√	7	5
26	30	F	L	Trauma	2	Proximal	BMAC	52	70	76	√		8	4
27	37	M	L	Trauma	2	Midsubstance	BMAC	54	64	86	√		6	5
28	25	M	R	Trauma	1	Proximal	BMAC	53	69	80	√		5	4
29	27	M	R	Trauma	1	Proximal	BMAC	58	65	75	√		6	4
30	29	F	L	Trauma	2	Midsubstance	BMAC	54	67	73	√		6	4

Conclusion

Overall, 95.0% of patients returned to sports at a mean follow-up of 3 mo. Mean time to return to sports was 3 months, the addition of BMAC shows promise in the treatment of grade 1, 2, and possibly grade 3 ACL tears without retraction. Further investigation using a controlled study design is warranted.

Conflict of Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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References

1. Sonnery-Cottet B, Colombet P. Partial tears of the anterior cruciate ligament. Orthop Traumatol Surg Res 2016;102:S59-S67. PMID: 26797008 DOI: 10.1016/j.otsr.2015.06.032.
2. Colombet P, Dejour D, Panisset JC, Siebold R; French Arthroscopy Society. Current concept of partial anterior cruciate ligament ruptures. Orthop Traumatol Surg Res 2010;96:S109-S118. PMID: 21056025 DOI: 10.1016/j.otsr.2010.09.003.
3. Dallo I, Chahla J, Mitchell JJ, Pascual-Garrido C, Feagin JA, LaPrade RF. Biologic Approaches for the Treatment of Partial Tears of the Anterior Cruciate Ligament: A Current Concepts Review.
4. Zicaro JP *et al.* ACL partial tears treated with PRP WJO https://www.wjgnet.com. June 18, 2021;6(12):431. Orthop J Sports Med 2017;5:2325967116681724. PMID: 28210653. DOI: 10.1177/2325967116681724.
5. DeFranco MJ, Bach BR Jr. A comprehensive review of partial anterior cruciate ligament tears. J Bone Joint Surg Am. 2009;91:198-208. PMID: 19122096. DOI: 10.2106/JBJS.H.00819
6. Zantop T, Brucker PU, Vidal A, Zelle BA, Fu FH. Intraarticular rupture pattern of the ACL. Clin Orthop Relat Res 2007;454:48-53. PMID: 17202917. DOI: 10.1097/BLO.0b013e31802ca45b
7. Crain EH, Fithian DC, Paxton EW, Luetzow WF. Variation in anterior cruciate ligament scar pattern: does the scar pattern affect anterior laxity in anterior cruciate ligament-deficient knees? Arthroscopy. 2005;21:19-24. PMID: 15650662. DOI: 10.1016/j.arthro.2004.09.015]
8. Noyes FR, Mooar LA, Moorman CT 3rd, McGinniss GH. Partial tears of the anterior cruciate ligament. Progression to complete ligament deficiency. J Bone Joint Surg Br. 1989;71:825-833. PMID: 2584255. DOI: 10.1302/0301-620X.71B5.2584255
9. Pujol N, Colombet P, Cucurulo T, Graveleau N, Hulet C, Panisset JC, *et al.* French Arthroscopy Society (SFA). Natural history of partial anterior cruciate ligament tears: a systematic literature review. Orthop Traumatol Surg Res. 2012;98:S160-S164. PMID: 23153663 DOI: 10.1016/j.otsr.2012.09.013
10. Fritschy D, Panoussopoulos A, Wallensten R, Peter R. Can we predict the outcome of a partial rupture of the anterior cruciate ligament? Knee Surg Sports Traumatol Arthrosc. 1997;5:2-5. PMID: 9127845 DOI: 10.1007/s001670050015
11. Bak K, Scavenius M, Hansen S, Nørring K, Jensen KH,

Jørgensen U. Isolated partial rupture of the anterior cruciate ligament. Long-term follow-up of 56 cases. Knee Surg Sports Traumatol Arthrosc. 1997;5:66-71. PMID: 9228310. DOI: 10.1007/s001670050028
12. Foster TE, Puskas BL, Mandelbaum BR, Gerhardt MB, Rodeo SA. Platelet-rich plasma: from basic science to clinical applications. Am J Sports Med. 2009;37:2259-2272. PMID: 19875361. DOI: 10.1177/0363546509349921
13. Lopez-Vidriero E, Goulding KA, Simon DA, Sanchez M, Johnson DH. The use of platelet-rich plasma in arthroscopy and sports medicine: optimizing the healing environment. Arthroscopy. 2010;26:269-278. PMID: 20141991. DOI: 10.1016/j.arthro.2009.11.015
14. Taylor DW, Petrera M, Hendry M, Theodoropoulos JS. A systematic review of the use of platelet rich plasma in sports medicine as a new treatment for tendon and ligament injuries. Clin J Sport Med. 2011;21:344-352 PMID: 21562414 DOI: 10.1097/JSM.0b013e31821d0f65
15. Figueroa D, Figueroa F, Calvo R, Vaisman A, Ahumada X, Arellano S. Platelet-rich plasma use in anterior cruciate ligament surgery: Systematic review of the literature. Arthroscopy. 2015;31:981-988. PMID: 25595696. DOI: 10.1016/j.arthro.2014.11.022]
16. LaPrade RF, Geeslin AG, Murray IR, Musahl V, Zlotnicki JP, Petrigliano F, *et al.* Biologic Treatments for Sports Injuries II Think Tank-Current Concepts, Future Research, and Barriers to Advancement, Part 1: Biologics Overview, Ligament Injury, Tendinopathy. Am J Sports Med. 2016;44:3270-3283. PMID: 27159318 DOI: 10.1177/0363546516634674
17. LaPrade RF, Goodrich LR, Phillips J, Dornan GJ, Turnbull TL, Hawes ML, *et al.* Use of Platelet-Rich Plasma Immediately After an Injury Did Not Improve Ligament Healing, and Increasing Platelet Concentrations Was Detrimental in an *In vivo* Animal Model. Am J Sports Med. 2018;46:702-712. PMID: 29211969. DOI: 10.1177/0363546517741135
18. Cole BJ, Seroyer ST, Filardo G, Bajaj S, Fortier LA. Platelet-rich plasma: Where are we now and where are we going? Sports Health. 2010;2:203-210. PMID: 23015939. DOI: 10.1177/1941738110366385
19. Nin JR, Gasque GM, Azcárate AV, Beola JD, Gonzalez MH. Has platelet-rich plasma any role in anterior cruciate ligament allograft healing? Arthroscopy 2009; 25:1206-1213 PMID: 19896041. DOI: 10.1016/j.arthro.2009.06.002
20. Di Matteo B, Loibl M, Andriolo L, Filardo G, Zellner J, Koch M, Angele P. Biologic agents for anterior cruciate ligament healing: A systematic review. World J Orthop 2016;7:592-603. PMID: 27672573. DOI: 10.5312/wjo.v7.i9.592]
21. Seijas R, Ares O, Cuscó X, Alvarez P, Steinbacher G, Cugat R. Partial anterior cruciate ligament tears treated with intraligamentary plasma rich in growth factors. World J Orthop. 2014;5:373-378. PMID: 25035842. DOI: 10.5312/wjo.v5.i3.373
22. Murray MM, Palmer M, Abreu E, Spindler KP, Zurakowski D, Fleming BC. Platelet-rich plasma alone is not sufficient to enhance suture repair of the ACL in skeletally immature animals: An *in vivo* study. J Orthop Res 2009;27:639-645 PMID: 18991345. DOI: 10.1002/jor.20796
23. You CK, Chou CL, Wu WT, Hsu YC. Nonoperative Choice of Anterior Cruciate Ligament Partial Tear: Ultrasound-Guided Platelet-Rich Plasma Injection. J Med Ultrasound. 2019;27:148-150. PMID: 31867179. DOI: 10.4103/JMU.JMU_121_18
24. Van Meer BL, Oei EH, Bierma-Zeinstra SM, Van Arkel ER, Verhaar JA, Reijman M, *et al.* Are magnetic resonance imaging recovery and laxity improvement possible after anterior cruciate ligament rupture in nonoperative treatment? Arthroscopy. 2014;1092-1099. PMID: 24951134. DOI: 10.1016/j.arthro.2014.04.098
25. Chahla J, Cinque ME, Piuzzi NS, Mannava S, Geeslin AG, Murray IR, *et al.* A Call for Standardization in Platelet-Rich Plasma Preparation Protocols and Composition Reporting: A Systematic Review of the Clinical Orthopaedic Literature. J Bone Joint Surg Am 2017;99:1769-1779. PMID: 29040132 DOI: 10.2106/JBJS.16.01374]
26. Jog AV, Smith TJ, Pipitone PS, Toorkey BC, Morgan CD, Bartolozzi AR. Is a Partial Anterior Cruciate Ligament Tear Truly Partial? Arthroscopy 2020; 36: 1706-1713 PMID: 32151662. DOI: 10.1016/j.arthro.2020.02.037
27. Van Dyck P, De Smet E, Veryser J, Lambrecht V, Gielen JL, Vanhoenacker FM, Dossche L, Parizel PM. Partial tear of the anterior cruciate ligament of the knee: injury patterns on MR imaging. Knee Surg Sports Traumatol Arthrosc 2012; 20: 256-261. PMID: 21773827. DOI: 10.1007/s00167-011-1617-7
28. Lehnert M, Eisenschenk A, Zellner A. Results of conservative treatment of partial tears of the anterior cruciate ligament. Int. Orthop. 1993;17:219-223. PMID: 8407036. DOI: 10.1007/BF00194182
29. Fruensgaard S, Johannsen HV. Incomplete ruptures of the anterior cruciate ligament. J Bone Joint Surg. Br 1989;71:526-530. PMID: 2722951. DOI: 10.1302/0301-620X.71B3.2722951
30. Centeno CJ, Pitts J, Al-Sayegh H, Freeman MD. Anterior cruciate ligament tears treated with percutaneous injection of autologous bone marrow nucleated cells: a case series. J Pain Res 2015;8:437-447. PMID: 26261424 DOI: 10.2147/JPR.S86244
31. Whitehead TS. Failure of anterior cruciate ligament reconstruction. Clin Sports Med. 2013;32(1):177-204.
32. Seijas R, Ares O, Cuscó X, Alvarez P, Steinbacher G, Cugat R. Partial anterior cruciate ligament tears treated with intraligamentary plasma rich in growth factors. World J Orthop. 2014;5(3):373-378.
33. Pujol N, Colombet P, Cucurulo T, *et al*; French Arthroscopy Society (SFA). Natural history of partial anterior cruciate ligament tears: A systematic literature review. Orthop Traumatol Surg Res. 2012;98(8 Suppl):S160-S164.
34. Georgoulis AD, Ristanis S, Moraiti CO, *et al.* ACL injury and reconstruction: Clinical related *in vivo* biomechanics. Orthop Traumatol Surg Res. 2010;96(8 Suppl):S119-S128.
35. Vavken P, Murray MM. Translational studies in anterior cruciate ligament repair. Tissue Eng Part B Rev. 2010;16(1):5–11.
36. Fisher MB, Liang R, Jung HJ, *et al.* Potential of healing a transected anterior cruciate ligament with genetically modified extracellular matrix bio scaffolds in a goat model. Knee Surg Sports Traumatol Arthrosc. 2012;20(7):1357-1365.
37. Vavken P, Murray MM. The potential for primary repair

of the ACL. Sports Med Arthrosc. 2011;19(1):44–49.
38. Kanaya A, Deie M, Adachi N, Nishimori M, Yanada S, Ochi M. Intraarticular injection of mesenchymal stromal cells in partially torn anterior cruciate ligaments in a rat model. Arthroscopy. 2007;23(6):610-617.
39. Wang H, Fleischli JE, Hutchinson ID, Zheng NN. Knee moment and shear force are correlated with femoral tunnel orientation after singlebundle anterior cruciate ligament reconstruction. Am J Sports Med. 2014;42(10): 2377-2385.
40. Li RT, Lorenz S, Xu Y, Harner CD, Fu FH, Irrgang JJ. Predictors of radiographic knee osteoarthritis after anterior cruciate ligament reconstruction. Am J Sports Med. 2011;39(12):2595-2603.
41. Sampson S, Botto-van Bemden A, Aufiero D. Autologous bone marrow concentrate: Review and application of a novel intra-articular orthobiologic for cartilage disease. Phys Sportsmed. 2013;41(3):7-18.
42. Paterno MV, Schmitt LC, Ford KR, *et al.* Biomechanical measures during landing and postural stability predict second anterior cruciate ligament injury after anterior cruciate ligament reconstruction and return to sport. Am J Sports Med. 2010;38(10):1968–1978.
43. Centeno CJ, Schultz JR, Cheever M, *et al.* Safety and complications reporting update on the re-implantation of culture-expanded mesenchymal stem cells using autologous platelet lysate technique. Curr Stem Cell Res Ther. 2011;6(4):368-378.
44. Centeno CJ, Busse D, Kisiday J, Keohan C, Freeman M, Karli D. Increased knee cartilage volume in degenerative joint disease using percutaneously implanted, autologous mesenchymal stem cells. Pain Physician. 2008;11(3):343–353.15.
45. Centeno CJ, Busse D, Kisiday J, Keohan C, Freeman M, Karli D. Regeneration of meniscus cartilage in a knee treated with percutaneously implanted autologous mesenchymal stem cells. Med Hypotheses. 2008;71(6):900-908.

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