

## Partial anterior cruciate ligament tears treated with intraligamentary plasma rich in growth factors

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### Abstract

**AIM:** To evaluate the effect of the application of plasma rich in growth factors (PRGF)-Endoret to the remaining intact bundle in partial anterior cruciate ligament (ACL) tears.

**METHODS:** A retrospective review of the rate of return to play in football players treated with the application of PRGF-Endoret in the remaining intact bundle in partial ACL injuries that underwent surgery for knee instability. Patients with knee instability requiring revision surgery for remnant ACL were selected. PRGF was applied in the wider part of posterolateral bundle and the time it took patients to return to their full sporting activities at the same level before the injury was evaluated.

**RESULTS:** A total of 19 patients were reviewed. Three had a Tegner activity level of 10 and the remaining 16

level 9. The time between the injury and the time of surgery was 5.78 wk (SD 1.57). In total, 81.75% (16/19) returned to the same pre-injury level of sport activity (Tegner 9-10). 17 males and 2 females were treated. The rate of associated injury was 68.42% meniscal lesions and 26.31% cartilage lesions. The KT-1000 values were normalized in all operated cases. One patient was not able to return to sport due to the extent of their cartilage lesions. The 15 patients with Tegner activity level 9 returned to play at an average of 16.20 wk (SD 1.44) while the 3 patients with Tegner activity level 10 did so in 12.33 wk (SD 1.11).

**CONCLUSION:** With one remaining intact bundle the application of PRGF-Endoret in instability cases due to partial ACL tear showed high return to sport rates at pre-injury level in professional football players.

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**Key words:** Anterior cruciate ligament; Plasma rich in growth factors; Platelet-rich plasma; Partial tears anterior cruciate ligament; Platelet-rich plasma

**Core tip:** The treatment with plasma rich in growth factors during an arthroscopy in cases of partial tears of ACL in soccer players could provide a restoration of function of the knee and return to play rates to pre injury levels in less than 4 mo.

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### INTRODUCTION

Anterior cruciate ligament (ACL) tears are common in

**Table 1** Inclusion and exclusion criteria for the review

Inclusion criteria	Exclusion criteria
Acute ruptures of the anterior cruciate ligament	Patients who were not active before the ACL injury
Active players competing in national and international teams (Tegner 9-10)	Patients with Tegner < 9
Clinic knee instability	Patients without evidence of instability (pivot shift more than 5 mm difference)
Magnetic resonance imaging of anterior cruciate ligament rupture	Ligaments with both bundles intact
Positive drawer	Ligaments with injury to both bundles or where the remaining bundle was clearly insufficient
One of the bundles intact	Infectious diseases, tumors, collagen, soft tissue or blood
First surgical procedure on evaluated knee	
Informed consent of the treatment	

ACL: Anterior cruciate ligament.

athletes and are often related to a non-contact pivoting injury mechanism in a deceleration maneuver<sup>[1,2]</sup>. The annual incidence in the United States is about 200000 cases with about 100000 treated with arthroscopic surgical procedures<sup>[3]</sup>. The symptoms have been described as a “pop” sensation and the development of an acute or subacute effusion. The clinical instability that often accompanies this injury limits sport activity especially contact-sports<sup>[1]</sup>.

Partial tears that predominantly affect one of the two major ACL bundles can also provoke conditions of pain and instability that pose a great challenge with respect to treatment, as treatment involves the preservation of the bundle that is found to be intact and its reinforcement with the objective of overcoming the symptoms that brought the patient to the operating room to begin with and return them to their sporting activity<sup>[2]</sup>.

The use of plasma rich in growth factors has proven useful in improving ligament maturation and specifically anterior cruciate ligament in vitro, in animals and in humans<sup>[4-6]</sup>.

The current study is a series of federated football players with a Tegner activity level of 9 and 10, who had suffered partial ACL injuries and underwent arthroscopic surgery for pain and instability and received PRGF-Endoret in the remaining intact bundle, assessing re-rupture and return to sport rates with such treatment.

## MATERIALS AND METHODS

A series of football players treated at the Mutualitat de Futbolistas Españoles, Barcelona Delegation, that underwent surgery for ACL injury during the 2009-2010 season were included in the study. The inclusion and exclusion criteria are described in Table 1.

A thorough check of patient medical history was performed on all patients and the time of injury was determined, as well as the moment at which they were unable to continue playing football, along with a physical examination including anterior drawer and pivot shift maneuvers. MRI was performed to confirm the ACL injury. The arthroscopic surgical procedure was performed by the same surgical team reviewing the intercondylar space and evaluating the integrity of the ACL bundles.

PRGF-Endoret was applied using the technique described by Anitua<sup>[7]</sup> (PRGF-Endoret) with a spine needle in both the proximal origin of the bundle and in the middle portion thereof in an amount of about 4 cc. At the end of the surgery when the articulation had been emptied and all surgical instruments had been removed another injection of PRGF-Endoret was administered (6 cc) in the articular space.

The knee was immobilized with a knee splint and maintained for 4 wk, with partial support from the affected limb and walking supported by 2 crutches. Upon completing this phase, the splint was removed permanently and progressive rehabilitation and physiotherapy was initiated with quadriceps strengthening exercises. At 6 wk post-op static bicycle exercises were initiated, at 8 wk elliptical trainer and at 12 wk running. The return to play was aimed at 16 wk post-op.

All patients underwent clinical follow up, MRI at 6 mo, anterior drawer, pivot shift and the time to return to play recorded.

## RESULTS

19 patients were reviewed aged between 20 and 32 years with a mean age of 25.52 years (SD 3.18). 17 men and 2 women, affecting 11 right and 8 left knees. Three cases were Tegner level 10 and the other 16 Tegner 9 (Table 2).

The time between the injury and the time of surgery was 5.78 wk (SD 1.57). No notable complications in any patients in the series, no obvious bleeding or infections.

All patients followed the protocols established for inclusion in this study. All patients were informed that they would be subjected to a diagnostic arthroscopy to assess the remnant ACL and in case of failure of both bundles, a reconstruction of the anterior cruciate with ipsilateral autologous graft from the central third of the patella ligament was performed.

The 19 cases presented complete rupture of the anteromedial bundle with an intact posterolateral bundle. In all cases the tension of the remnant bundle was tested by a senior surgeon with over 30 years' experience in ligamentoplasty. If the remaining bundle failed the test, reconstruction was performed using autologous patellar

**Table 2** Epidemiological data

No.	Age	Tegner	RTP wk	KT-1000 pre	KT-1000 post	TTS wk
1	24	9	15	3	1	7
2	23	9	16	3	0	6
3	27	9	15	2	0	7
4	29	9	17	2	0	8
5	21	9	14	4	1	6
6	22	9	15	3	0	7
7	28	10	12	3	0	2
8	32	9	-	5	2	5
9	31	9	15	4	1	6
10	25	10	11	3	0	1
11	20	9	14	4	1	6
12	23	10	14	3	0	1
13	21	9	15	3	0	7
14	27	9	17	4	1	8
15	29	9	18	3	0	5
16	24	9	17	2	0	8
17	27	9	19	2	0	7
18	30	9	20	3	1	7
19	22	9	16	2	1	6

RTP: Return to play; TTS: Time to surgery; KT-1000: Difference between both knees.

graft. In the 19 cases examined remnant bundles were determined as intact with sufficient tension and PRGF was applied as previously described.

During surgery, associated injuries were observed in 68.42% of the cases (21.04% medial meniscus, 36.84% lateral meniscus, and 10.52% bilateral) with cartilage injuries in 26.31% all of which in the medial femoral condyle cartilage.

Of the 19 cases, the 3 patients with Tegner activity level 10 returned to play at pre-injury level. Of the remaining 16 patients with Tegner activity level 9, three (18.75 %) cases were not able to return to the same level of competition. Of these, one re-ruptured his ACL at 7 mo after surgery upon resuming normal training at competition level, another re-ruptured the ACL at 22 mo post-surgery competing at pre-injury level and the third presented meniscal and cartilage lesions that prevented him from reaching his pre-injury level of fitness due to the discomfort and pain these injuries provoke (although without evident instability).

The 15 patients with Tegner activity level 9 returned to play at an average of 16.20 wk (SD 1.44) while the 3 patients with Tegner activity level 10 did so in 12.33 wk (SD 1.11). Apart from the 3 cases described above and two players who voluntarily left their sport for personal reasons, at 2 years follow up there were no new signs of instability in all players, all of them able to reach and maintain their pre-injury level of competition.

MRI study was performed in all cases, observing the remnant anterior cruciate ligament bundle with complete ligamentization at 1 year post-surgery and good anatomical arrangement.

## DISCUSSION

The application of PRGF-Endoret in the remnant ACL

allowed for an early return to play in partial ACL injuries in Federated and Professional Footballers.

The ACL has been described basically as having two functional bundles<sup>[8-10]</sup>, the anteromedial bundle (AM) and posterolateral (PL). From a biomechanical point of view the AM resists anterior drawer displacement of between 60° and 90° while the PL does the same near full knee extension<sup>[9]</sup>.

Partial ACL tears compromise one of the two bundles. In previous works it has been pointed out how ruptures to one of the two bundles are produced<sup>[11]</sup> also linking the relationship between the ACL and rotational stability. While Furman published in 1976 that the ACL provided stability in anterior translation mechanisms<sup>[12]</sup>, more recent studies insist that rotational instability is closely related to the PL bundle<sup>[13]</sup> and this situation translates into maneuvers like the positive pivot shift. This same situation occurs in ACL reconstructions with femoral tunnel positioned excessively vertical (11- to 1-o' clock) when the anterior displacement maneuvers can be negative (anterior drawer, Lachman test) while the pivot shift is positive<sup>[10]</sup>.

Different authors have published figures on the occurrence of partial ACL lesions to be between 10% and 38%<sup>[8,14,15]</sup>, although the figures for partial ACL lesions symptomatic in surgeries are situated between 5% and 14% of the total for ACL lesions<sup>[11,16-19]</sup>.

The natural history of ACL total rupture has been described previously and is estimated at causing a risk of instability in 15% to 66 % of patients and 15% to 86% risk of meniscal tear<sup>[20]</sup>. The natural history of knees with partial ACL tear has not been described sufficiently, although the review by Pujol *et al*<sup>[18]</sup>, which was based on previously published studies and collecting more than 400 patients, concluded that partial ACL tear offers good functional results short to medium term, especially when limiting patients' physical activities<sup>[18]</sup>. Since these patients have residual pain especially when exerting themselves, even without a subjective feeling of instability, a surgical approach is recommended<sup>[18]</sup>. The proportion of patients who return to play at pre- injury level without undergoing surgery is estimated to be between 30% and 44% of patients with follow-up of 18 mo to 5 years<sup>[21,22]</sup>.

Some authors have also described the proportion of partial ACL tears that become complete ruptures to be between 38 and 50%, possibly related to necrosis at the injury site after vascular injury to the remnant ACL<sup>[14,23,24]</sup>.

These data have inspired various specialists to find alternative surgical solutions. In many cases total reconstruction is opted for<sup>[25]</sup> sacrificing the remnant intact ACL bundle and performing a standard ligamentoplasty with Bone-Tendon-Bone or hamstrings.

Cases that opted for retensioning of the tissue with Electrothermal shrinkage<sup>[26]</sup>. have not proven to be successful.

This has led different authors to consider the reconstruction of one of the two bundles, typically the AM, in the presence of the integrity of the other bundle<sup>[10,11]</sup>.

The use of biological therapies has seen an increase in

recent years, especially the use of plasma rich in growth factors (PRGF). The application of PRGF in various tissues, especially the ACL, has been the focus of several studies, which have not only shown structurally improved tissues but also enhanced ACL graft healing<sup>[5,6]</sup>, or even in the autologous central third patellar tendon harvest site<sup>[27-30]</sup>. The role of PRGF has been linked to the regeneration processes such as angiogenesis, cell activation and differentiation and stem cells<sup>[31,32]</sup>. Several studies have shown improvement to processes such as neovascularization and angiogenesis in tendon and ligament tissue with increased tenocytes<sup>[33-40]</sup>, increased tissue strength in animals<sup>[29,30,41-46]</sup> and human studies with early return to competition level sport and early maturation of ligaments and tendons, and a reduction in pain<sup>[27,28,47-49]</sup>. It is important to point out that findings from both clinical studies and tissue studies coincide on the importance of the role of platelet-rich plasma (PRP) in the early phase of repair, and this is precisely where to look for differences in the control groups<sup>[50-53]</sup>.

The main limitation of the current study is the lack of similar studies to this one and therefore lack of comparisons with other series. Another significant limitation is the lack of a control group that would have received physiological saline solution in the remnant ACL bundle to assess changes after a simple stimulus puncture. This lack of control group impedes the quantification of the impact of surgery simply for the influence of surgery on the knee without even considering the role of PRGF. In the design of this review no functional assessments were performed and no scores were taken, which could have improved the quality of this study.

Possible studies that could follow this one should definitely include the design of a clinical trial with a control group to assess the natural history of partial ACL ruptures, and a functional assessment, although early functional tests in the first mo are recommended as this is when changes in the groups receiving PRGF are to be expected as it accelerates the healing and tissue regeneration processes.

One remaining intact bundle and the application of PRGF-Endoret in instability cases due to partial ACL tear in professional football players with Tegner activity levels 9 and 10, provides sufficient stability for the return to play at pre-injury level.

## COMMENTS

### Background

Partial anterior cruciate ligament (ACL) tears are a therapeutic challenge. Biological treatments have shown an acceleration of the processes of regeneration and repair. The use of biologic therapies to repair instabilities due to partial tears may be an alternative to surgical augmentation plasty.

### Research frontiers

The use of plasma rich in growth factors (PRGF) can be an effective treatment for partial ACL tears during revision arthroscopy avoiding the necessity for reconstruction of the injured fascicle.

### Innovations and breakthroughs

The use of PRGF has been reported in the regeneration of cartilage and ligaments. It has been shown to accelerate the phases of plasty maturation and/or

ligamentization. There is no prior publication similar to this, offering a new therapeutic possibility for this problem.

### Applications

It is clear that this is a preliminary study and may give rise to a clinical trial to evaluate the impact of using PRGF in partial ACL tears.

### Terminology

PRGF is plasma rich in growth factors, one of the ways of obtaining platelet-rich plasma. PRGF's role in accelerating the regeneration of tissues has been demonstrated, including ligaments and tendons.

### Peer review

The fact that patient's return to play at pre-injury level was assessed gives us a clear indication of the degree of improvement in these patients from a clinical point of view. Their full return to sport at pre-injury level is objective data on their improvement.

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