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This prospective pilot study evaluated the efficacy of using the growth factors found in platelet rich plasma (PRP) as a potential treatment in anterior cruciate ligament (ACL) surgery.

Methods

- Twenty patients with laxity caused by torn ACL underwent arthroscopically assisted reconstruction with autologous quadrupled hamstring tendon graft (QHTG).
- The platelet gel was applied in the femoral and tibial tunnels.
- The rehabilitation protocol was standardized for both groups and included
  - Immediate postoperative mobilization without a knee brace
  - Protected weight bearing for 3 weeks
  - Return to sporting activities at 6 months
- At 6 months, patients were evaluated both clinically and functionally
  - KOOS, knee injury and osteoarthritis outcome scores
  - KT-1000, instrumented measurement of anterior laxity of the knee
  - Tegner scale rating
  - Clinical examination
  - Computed tomography (CT) of the knee with limited number of patients undergoing magnetic resonance imaging (MRI)

Results

- At 6 months after ACL surgery,
  - The PRP Group and Control groups showed no significant differences concerning KOOS, KT-1000, Tegner score, and clinical examination
  - CT scans highlighted a significant difference ($p < 0.01$) between ACL density of the two groups.
    - CT densities of the ACL and posterior cruciate ligament (PCL) were similar in the PRP treated group
      - In the control group, the intensity of the signal was heterogeneous and the new ACL was not clearly identifiable with respect to the PCL
    - The ACL density between the PRP treated group and control group was noticeably different
      - In the PRP treated group, the density was uniform and the new ACL was more structured
      - In the Control group, the ligament was less structured and did not completely fill the femoral and tibial tunnels

Conclusions/Key Points

- CT data showed that the transformation from autologous QHTG to new ACL was faster in the PRP group than the controls.
- Growth factors from PRP may accelerate the integration of the new ACL in the femoral and tibial tunnels.

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Use of growth factors in ACL surgery: preliminary study

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Abstract There is no general consensus on the use of growth factors (GF) in surgery. The aim of this study was to clarify if GF play a role in anterior cruciate ligament (ACL) surgery. Twenty patients with laxity caused by a torn ACL underwent arthroscopically assisted reconstruction with autologous hamstring tendons. We performed a prospective study with these patients randomized into 2 groups: GF-treated and control. Growth factors were obtained according to the GPS Biomet-Merck technique and are applied to femoral and tibial tunnels during surgical procedure. Patients were evaluated clinically and functionally. Computed tomography (CT) of the knee was performed in all the patients; a limited number of patients underwent magnetic resonance imaging (MRI). There were no significant differences concerning KOOS, IKDC, KT-1000, Tegner score rating and clinical examination between the two groups 6 months after ACL surgery. CT highlighted a significant difference ($p<0.01$) between ACL density of the two groups and showed that ACL density was similar to that of the posterior cruciate ligament in GF-treated group. In this group, however, one patient had a synovitic reaction: the new ACL was increased, hypertrophic and surrounded by a reaction of soft tissues. GF may accelerate the integration of the new ACL in the femoral and tibial tunnels, but further clinical studies are necessary to better understand the mechanism of action of GF, widely studied only in vitro and in animal models.

Key words ACL • Arthroscopy • Hamstring tendons • Growth factors • Sporting activities

Introduction

Lesions of anterior cruciate ligament (ACL) represent one of the most common traumas in sporting practice (75 000–100 000 cases/year in USA) [1] and have shown a tendency to increase in the last few years. This increase is probably due to the great number of middle-aged subjects who practise sports and to the diffusion of sporting activities at high risk for knee trauma.

The loss of the knee centre rotation following ACL lesions causes a functional overload, leading to cartilage defects, meniscal lesions and early gonarthritis. Adequate treatment must be prescribed according to the single demands and the patient's characteristics [2].

At present, various surgical techniques exist for the reconstruction of ACL with autologous tendon, and provide good clinical results with resumption of the sporting activity.

In our clinical practice, we prefer to reconstruct the ACL with quadrupled hamstring tendon graft (QHTG).

QHTG technique is at least an equivalent option to the bone-patellar tendon-bone graft for ACL reconstruction. QHTG has the advantage of maintaining the integrity of the extensor apparatus of the knee [3]. Patients progressively resume sporting activities with full recovery 6 months after surgical procedure.

Use of growth factors in ACL surgery may shorten the post-operative rehabilitation and the time necessary to resume sporting activities [4]. Growth factors may accelerate the bony integration of QHTG and the process of transformation from autologous tendons to new ACL.

However, the literature reports controversial data that confirm or deny the effectiveness of this procedure [5, 6]. Therefore, we studied the effects of growth factors in ACL surgery with QHTG.

Materials and methods

Twenty patients with laxity caused by a torn ACL underwent arthroscopically assisted reconstruction with QHTG. The surgical procedure was performed by the same surgeon. Fixation of QHTG was made with reabsorbable devices: femoral transcondylic fixation (Bio-Trans Fix, Arthrex) and tibial interference screw (BioRCI, Smith & Nephew). We performed a prospective study with these patients by randomizing them into 2 groups: patients treated with growth factors (GF-treated) and patients treated without growth factors (control).

Growth factors were obtained according to the GPS Biomet-Merck technique (Biomet Inc., Warsaw, Indiana), in which the growth factors, maximally concentrated in platelets, are obtained from the combination of a plateleted gel and autologous thrombin. Plateled gel and autologous thrombin are injected separately and in the sametime. They are combined directly in the bone tunnels The gel is obtained from 54 ml autologous blood and 6 ml of citric acid. Platelet rich plasma (PRP) is obtained after centrifugation at 3200 RPM for 12 minutes. Autologous thrombin is obtained from 20 ml autologous blood, left for 5 minutes at room temperature for coagulation followed by centrifugation at 3200 RPM for 2.5 min.

Growth factors thus prepared are applied in femoral and tibial tunnels during surgical procedure.

The rehabilitation protocol used in GF-treated and control groups was standardized. This protocol included immediate post-operative mobilization without a knee brace, protected weight bearing for 3 weeks, and return to sporting activities at 6 months.

Patients were evaluated 6 months after surgery both clinically and functionally:

- Knee injury and osteoarthritis outcome score (KOOS) [7], based on a self-administered outcome measure, including knee function, daily and sporting activities and quality of life. A value of 0 is abnormal while 100 refers to a healthy knee.
- Instrumented measurement of anterior laxity of the knee with KT-1000 [8].
- Tegner scale rating [9].
- Clinical examination (performed by the same physician).

Computed tomography (CT) of the knee was performed in all the patients. A limited number of patients underwent magnetic resonance imaging (MRI).

Data were analysed statistically with the Mann-Whitney test.

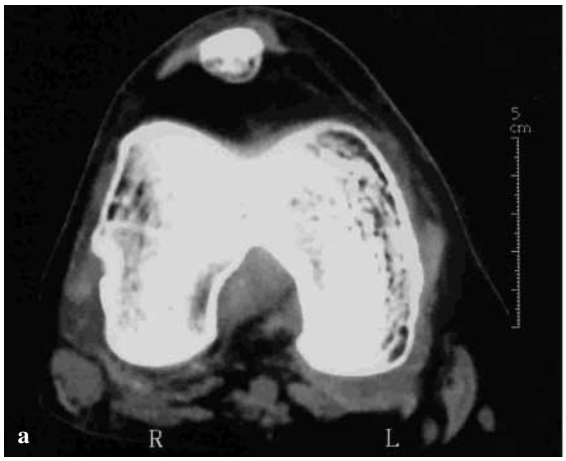
Results

A total of 20 patients with anterior cruciate ligament (ACL) injuries were treated by quadrupled hamstring tendon graft (QHTG) with or without growth factor (GF) application. The 2 groups were similar for age, gender and sporting activity levels (Table 1). There were no significant differences concerning KOOS, KT1000, Tegner score and clinical examination results between the two groups 6 months after ACL surgery. Measurement of quadriceps circumference showed a difference between healthy and operated limbs in the same patient of 1.3±1.2 cm in GF-treated group vs. 1.8 ±1.2 cm in the control group.

Table 1 Clinical and functional outcomes 6 months after surgery in 20 patients who underwent quadrupled hamstring tendon graft (QHTG) for sports-related torn anterior cruciate ligament, by treatment group. Patients treated with growth factors (GF) received platelet-rich plasma and autologous thrombin during surgery. Values are mean (SD) unless otherwise indicated. No difference between groups is significant

	GF-treated (n=10)	Control (n=10)
Age at treatment, years	36.6 (9.3)	30.2 (5.3)
Male, n (%)	9 (90)	9 (90)
Functional evaluations		
KOOS	83 (20)	84 (9)
KT-1000 difference, mm[a]	0.8 (1.4)	1.2 (0.9)
Tegner score difference[b]	0.9 (2.0)	0.8 (0.9)
Clinical evaluations, n (%)		
Swelling	0 (0)	1 (10)
Maximun flexion		
60°	0 (0)	0 (0)
90°	0 (0)	0 (0)
120°	2 (20)	1 (10)
>120°	8 (80)	9 (90)
Extension deficit	3 (30)	0 (0)
Maniscal test (negative)	8 (80)	8 (80)
Patellar test (negative)	7 (70)	6 (60)
Anterior drawer test (negative)	9 (90)	10 (100)
Lachman test (negative)	9 (90)	9 (90)

KOOS, Knee injury and osteoarthritis outcome score
[a] Between healthy and operated limbs; [b] Between preoperative and postoperative sports activities



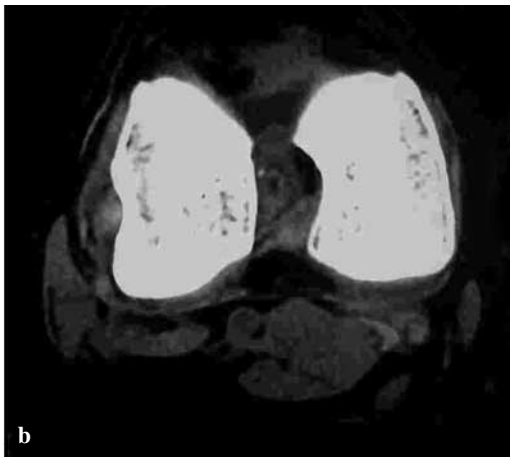


Fig. 1a, b *Representative computed tomography (CT) scans of patients treated with quadrupled hamstring tendon graft (QHTG) for anterior cruciate ligament injury.* **a** Patient in the growth factor treatment group. **b** Patient in control group

Table 2 CT measure ACL density (expressed by Huasfield). Statistical analysis (Main-Whitney Test)

GF-Treated	Control
86.0	82.0
71.9	104.1
81.8	88.0
100.7	97.2
90.4	96.6
75.3	95.1
88.1	90.8
67.6	107.1
82.7	95.1

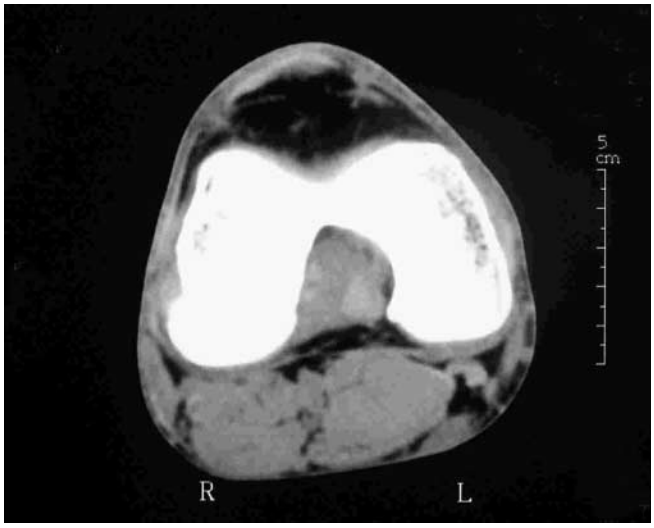


Fig. 2 CT scan of the anterior cruciate ligament in a patient assigned to the growth factor treatment group. This patient experienced a synovitic reaction

Interesting data were obtained from the evaluation of the knee with CT and MRI. CT highlighted a significant difference ($p<0.01$) between ACL density of the two groups. CT densities of the ACL and posterior cruciate ligament (PCL) were similar in GF-treated group (Fig. 1a). In the control group, instead, the intensity of the signal was heterogeneous and the new ACL was not clearly identifiable with respect to the PCL (Fig. 1b). Similarly, we noticed a different density of the ACL: in the GF-treated group this density was uniform and the new ACL was more structured, while in the control group the ligament was less structured and did not completely fill the femoral and tibial tunnels.

The presence of bony sclerosis hindered any consideration concerning tendon-bone integration (Table 2). In the GF-treated group one patient had a synovitic reaction. On CT, the new ACL was increased and hypertrophic and surrounded by a soft-tissue reaction. MRI confirmed these observation (Fig. 2).

Discussion

Growth factors have effects on several tissues, but it is still unclear how favourable is their use in surgical practice [4]. These is no consensus regarding the use of growth factors in ACL surgery [5, 6].

The structure of the ACL becomes tendon-like 9–12 months after surgery. We observed that the transformation from autologous QHTG to new ACL was faster in the GF-treated group than in controls. Therefore GF could accelerate the integration of the new ACL in the femoral and tibial tunnels. CT data confirmed our hypothesis.

These data are interesting for the sporting outcome. Resumption of sporting activities after ACL surgery employing GF will be shorter if our data are confirmed by

other studies. At present the principal limit of GF technique is that we do not know how widely the GF are able to promote cellular replication and differentiation. Furthermore, the synovitic reaction observed in one patient of GF-treated group stresses the need for further studies. In particular, clinical studies are required to better understand the mechanism of action of GF, widely studied only in vitro and in animal models.

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