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The impact of platelet-rich plasma on the prevention of tunnel widening in anterior cruciate ligament reconstruction using quadrupled autologous hamstring tendon

A RANDOMISED CLINICAL TRIAL

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The use of platelet-rich plasma (PRP) as an adjuvant to tissue repair is gaining favour in orthopaedic surgery. Tunnel widening after anterior cruciate ligament (ACL) reconstruction is a recognised phenomenon that could compromise revision surgery. The purpose of this study was to determine whether PRP might prevent tunnel widening in ACL reconstruction.

Patients undergoing ACL reconstruction using a hamstring graft were randomly allocated either to have PRP introduced into the tunnels peri-operatively or not. CT scanning of the knees was carried out on the day after surgery and at three months post-operatively and the width of the tunnels was measured. Patients were also evaluated clinically at three months, when laxity was also measured.

Each group comprised 25 patients, and at three months post-operatively all were pain-free with stable knees, a negative Lachman test and a good range of movement. Arthrometric results had improved significantly in both groups ($p < 0.001$). Despite slightly less tunnel widening in the PRP group, there was no significant difference between the groups at the femoral opening or the mid-tunnel ($p = 0.370$ and $p = 0.363$, respectively) nor at the tibial opening or mid-tunnel ($p = 0.333$ and $p = 0.177$, respectively).

We conclude that PRP has no significant effect in preventing tunnel widening after ACL reconstruction.

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After anterior cruciate ligament (ACL) reconstruction the tunnels accommodating the graft enlarge in between 25% and 100% of cases.[1-4] Although this may not significantly affect the initial outcome, it may be difficult to perform a single-stage procedure if revision surgery is required.[5-8]

It is thought that a variety of biological and biomechanical factors contribute to widening of the tunnel, although the aetiology is poorly understood.[9] Osteolytic cytokines, including interleukin (IL)-β1, IL-6, bone morphogenic protein (BMP), tumour necrosis factor-α (TNF-α), and nitric oxide play a role.[10] Graft selection, the method of fixation, the amount of movement of the graft in the tunnel, heat necrosis as a result of drilling and an aggressive rehabilitation programme may be contributing factors.[3,11] Most studies have demonstrated that tunnel widening is more evident following hamstring than bone–patellar tendon–bone grafts.[6,8,11-13] Jagodzinski et al[11] found more widening with the use of a bio-absorbable interference screw than with press-fit fixation with an autologous bone plug. Silva et al[5] proposed that biological factors have a greater impact on the process of widening, but most studies favour mechanical factors.[6,9]

Platelet-rich plasma (PRP) containing various growth factors and cytokines may encourage the healing of bone, cartilage, muscle, tendon and ligamentous tissue, and has been used as an adjunct in various orthopaedic procedures, including ACL reconstruction.[14-17] Beneficial effects on the incorporation of tendon grafts have been demonstrated.[18,19] This study assesses the effect of PRP in reducing the widening of both the femoral and tibial tunnels after single-bundle arthroscopic ACL reconstruction using a quadrupled autograft of hamstrings.

Patients and Methods

In a prospective randomised clinical study over one year (February 2011 to February 2012), patients with non-acute ACL injury admitted for reconstructive surgery were recruited. The inclusion criteria were an isolated ACL tear without any other ligament injury, age between

Fig. 1a

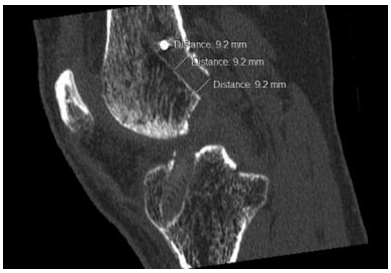

Fig. 1b

CT scans in a patient not receiving platelet-rich plasma a) on the first post-operative day and b) at three months post-operatively, showing the diameter of the femoral tunnel.

18 and 40 years, no previous knee surgery, and a normal range of movement in the affected knee without demonstrable degenerative joint changes on plain radiographs. The study had ethical approval and all patients gave informed consent.

A total of 50 patients with an isolated ACL injury diagnosed by clinical examination and MRI were included. All underwent arthroscopic single-bundle reconstruction using a hamstring quadrupled graft and a transfix system of fixation (Arthrex; Arthrex Inc., Naples, Florida) was used. They were allocated into one of two groups according to random numbers generated via a random number table. Group A had PRP injected into the tunnels at the time of surgery and group B did not. All operations were performed by the same surgeon (FM).

The PRP was prepared using a double syringe system (Arthrex) and 10 ml of the patient's blood was centrifuged at 1500 rpm for five minutes, from which 3.5 ml of PRP was obtained. The graft was immersed in the PRP solution for approximately five minutes before implantation. After removing the graft from the solution the residual volume was less than half, indicating that the PRP was absorbed into the graft. The diameter of the graft was measured to the nearest millimetre, and tunnels were drilled to the appropriate size.

The femoral tunnel was fashioned through an anteromedial portal and the tibial tunnel along a guide wire inserted from the anteromedial tibia 3 cm below the joint line, with a 55° sagittal and 70° coronal inclination, breaching the tibial plateau just medial to the anterior horn of the lateral meniscus. The graft was fixed in the femoral tunnel by a cross-pin and in the tibial tunnel by a bio-absorbable interference screw one size larger than the diameter of the graft. At the completion of surgery, in the PRP group fluid was evacuated from the knee and, using a dry arthroscopic technique, an 18 gauge spinal needle was positioned in the tunnel; 2 ml of PRP were then injected into the femoral tunnel and 1.5 ml into the tibial tunnel. Post-operatively all patients wore a knee immobiliser in full extension for two weeks, and all followed the same rehabilitation protocol.

On the day after operation, and three months later, when the maximum widening occurs,[20-22] CT scans were undertaken and the diameter at the aperture and in the middle of the tunnels was measured using the Siemens Emotion six-slice multidetector CT (Siemens, Erlangen, Germany) (Fig. 1). All were calculated in millimetres using the auto-calibrated software. Correlation between these data and the diameter of the reamers was checked in the first few cases and the difference was found to be negligible. The percentage of widening was defined as the difference in the measurements between the two time periods. Significant widening was defined as an increase > 2 mm.[6,12]

All patients were also examined clinically three months post-operatively by an author (MTA), and the range of movement (ROM) of the knee, stability and pain (on a visual analogue scale) were recorded. Stability was assessed using the KT-1000 arthrometer (MEDmetric Corp., San Diego, California).

Statistical analysis. The software package PASW statistics 18 (SPSS Inc., Chicago, Illinois), was used to analyse the data using the Kolmogorov-Smirnov test, which showed normal distribution of all data. The *t*-test and Pearson's chi-squared test were used to compare mean values between the groups. Statistical significance was set at a p-value < 0.05.

Results

Of the 50 patients, four (two in each group) were lost to follow-up, leaving 23 patients in each group. In the PRP group there were 20 men and three women with a mean age of 26.4 years (18 to 40), and in the control group there were 22 men and one woman with a mean age of 26.9 years (18 to 40). Additional surgery was carried out in the form of four meniscectomies and one meniscal repair in the PRP group, and three meniscectomies in the control group.

Table I. Mean widening of the apertures and mid-sections of the femoral and tibial tunnels (PRP, platelet-rich plasma)

Variable	n	Mean (SD) tunnel widening at three months (mm)	Mean (SD) tunnel widening at three months (%)
Femoral tunnel opening			
PRP group	23	2.16 (1.37)	27.35 (18.32)
Control group	23	2.50 (1.22)	31.39 (16.80)
p-value		0.441	0.370
Mid-femoral tunnel			
PRP group	23	2.69 (2.06)	34.27 (27.37)
Control group	23	3.21 (1.72)	40.34 (22.45)
p-value		0.415	0.363
Tibial tunnel opening			
PRP group	23	1.65 (0.98)	18.95 (12.04)
Control group	23	1.99 (1.31)	24.45 (17.69)
p-value		0.225	0.333
Mid-tibial tunnel			
PRP group	23	2.09 (1.52)	22.18 (17.16)
Control group	23	2.70 (1.48)	28.62 (16.85)
p-value		0.206	0.177

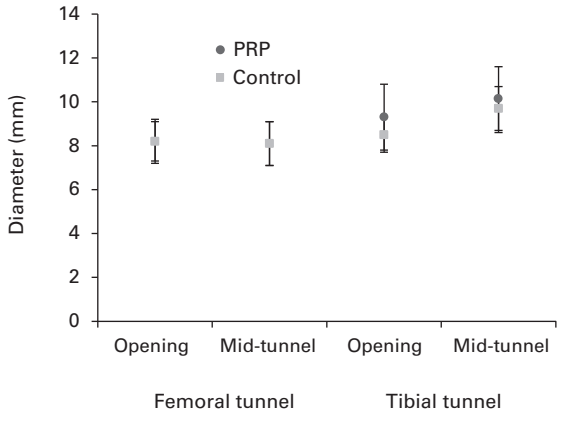

Fig. 2a

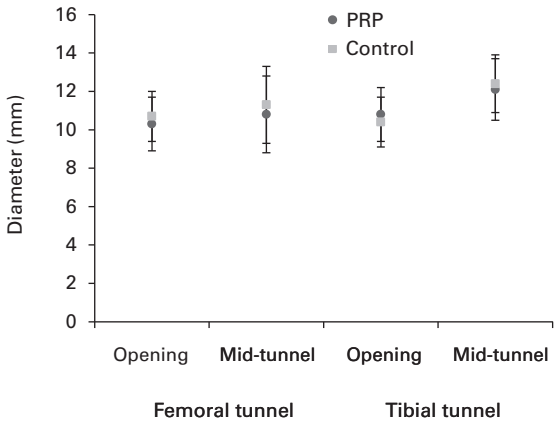

Fig. 2b

Graphs showing the mean diameters of the femoral and tibial tunnels (openings and mid-tunnels) in the platelet-rich plasma (PRP) and control groups a) on the first post-operative day and b) at three-months post-operatively. The error bars denote the standard deviation.

Despite slightly less tunnel widening in the PRP group, there were no significant differences at any of the sites of measurement between immediately after surgery and three months post-operatively. Although there was significant widening in both groups, there was no difference between the two groups (Table I; Figs 2 and 3).

Pre-operatively, the difference between the antero-posterior excursion, as measured by the KT-1000 arthrometer, between the operated and the normal knee was a mean of 6.6 mm (5 to 9; SD 1.3) in the PRP group and 6.6 mm (4 to 9; SD 1.5) in the control group. At three months these values had improved to 1.1 mm (0 to 3; SD 0.9) in the PRP group and 2.2 mm (0 to 4; SD 1.1) in the control group, which was significant in both groups (both $p < 0.001$).

One patient in the control group required a manipulation under general anaesthesia for limitation of movement. No other complications occurred in either group. At three months follow-up all patients in both groups had a negative Lachman test, a stable knee with no pain and a good ROM.

Discussion

Radiological widening of tunnels after ACL reconstruction is a well described phenomenon. We found that PRP, despite its recognised properties, had no effect on tunnel

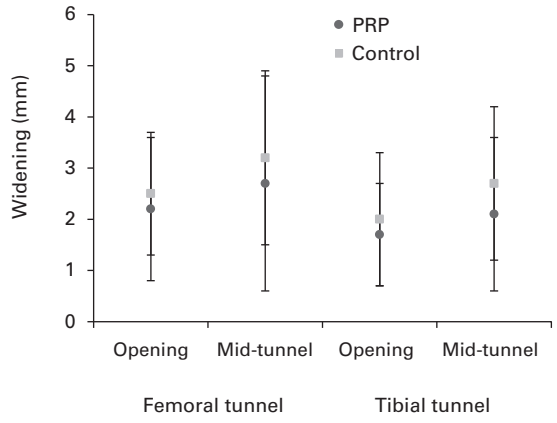

Fig. 3a

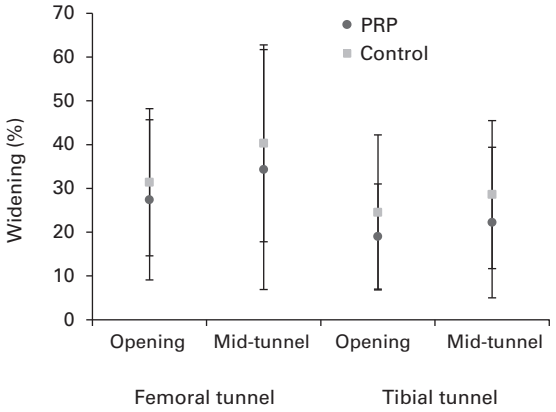

Fig. 3b

Graphs showing the mean widening of the femoral and tibial tunnels (openings and mid-tunnels) in a) millimetres and b) percentage in the platelet-rich plasma (PRP) and control groups. The error bars denote the standard deviation.

widening following ACL surgery in the short term. Our results confirmed that despite a significant degree of widening in some patients, it did not prejudice the clinical outcome at three months.

It has been clearly demonstrated that PRP enhances tissue repair by releasing growth factors.[15-17,23-25] Several authors have shown that PRP improves the ligamentous anchorage of ACL reconstruction grafts, but the clinical significance has been questioned.[18,19]

An important limitation of this study is the lack of objective measurement of the concentration of PRP in tunnels, which is technically demanding. To be more confident of an acceptable concentration of PRP in the tunnels and to avoid any dilutional effect of joint washout, we evacuated all the fluid from the knee at the time of injecting the PRP. In practice, we were uncertain about whether we really delivered PRP accurately into the tunnels, and in an attempt to improve this we used a large spinal needle placed at the femoral tunnel opening under arthroscopic control. We derived comfort from the findings of Sanchez et al,[25] who recorded that even the one-third concentration of PRP we produced, delivered into the surgical field, is enough to exert an effect.

Our study shows only a slight reduction in tunnel widening using PRP, which did not reach statistical significance. Thus, on this evidence, we cannot currently recommend the routine use of PRP at the time of ACL reconstruction for the prevention of tunnel widening.

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