Orthopaedics & Traumatology: Surgery & Research 105 (2019) 653–660

Contents lists available at ScienceDirect

Orthopaedics & Traumatology: Surgery & Research

journal homepage: www.elsevier.com

Original article

Morphological changes in the femoral and tibial bone tunnels after anatomic single-bundle anterior cruciate ligament reconstruction using a calcium phosphate-hybridized tendon graft in 2 years of follow-up

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ARTICLE INFO

Article history:
Received 29 May 2018
Accepted 9 January 2019

Keywords:
Anatomic single-bundle anterior cruciate ligament reconstruction
Calcium phosphate hybridization
Bone tunnel enlargement
Morphological change
Computed tomography

ABSTRACT

Introduction: A calcium phosphate (CaP)-hybridized tendon graft improves tendon-to-bone healing. The purpose of the study was to evaluate the progression of morphological changes in the femoral and tibial bone tunnels after anatomic single-bundle anterior cruciate ligament (ACL) reconstruction using the CaP-hybridized tendon graft versus an untreated tendon graft during 2 years of follow-up.
Hypothesis: We hypothesized that the CaP-hybridized tendon graft would prevent the progression of bone tunnel enlargement compared with the untreated tendon graft.
Patients and methods: The CaP group comprised 19 patients, while the conventional group comprised 18. Computed tomography was performed at postoperative 1 week, 1 year, and 2 years. The bone tunnel enlargement and tunnel translation at the aperture of the femoral and tibial tunnels were analyzed.
Results: In the CaP group, the femoral bone tunnel did not expand during 2 years of follow-up. In the conventional group, the femoral bone tunnel diameters at postoperative 1 year and 2 years were enlarged compared with postoperative 1 week, and the proximal and distal walls of the femoral bone tunnel shifted proximally and distally, respectively. The femoral bone tunnel in the CaP group was smaller than that in the conventional group at 1 year postoperatively. Although the tibial bone tunnels expanded for up to 1 year postoperatively in both groups, the expanded bone tunnel reduced during 2 years of follow-up only in the CaP group.
Discussion: In anatomic single-bundle ACL reconstruction, the femoral bone tunnel in the CaP group did not expand or progress with time compared with the conventional group, while the tibial bone tunnel in the CaP group expanded for up to 1 year postoperatively and then reduced for up to 2 years postoperatively. The CaP-hybridized tendon can prevent the progression of bone tunnel enlargement.
Level of evidence: Level II, Low-powered prospective randomized trial.

1. Introduction

To improve tendon-to-bone healing, we developed a novel technique that involved hybridizing calcium phosphate (CaP) with tendon grafts using an alternate soaking process [1]. The CaP-hybridized tendons are created by alternately soaking the tendon graft in a calcium solution for 30 s, followed by a phosphate solution for 30 s, and repeating this process ten times [2–4]. In the CaP-hybridized tendon, needle-like CaP crystals 30 to 50 nm in length (low-crystalline apatite) are deposited on and between collagen fibrils from the surface to 200 μm deep in the tendon [2,3]. The CaP-hybridized tendon resembles the microstructure of bone that contains apatite and type I collagen. Using the CaP-hybridized tendon results in scarless direct bonding between the grafted tendon and the newly formed bone at 2 to 3 weeks after implantation in a bone tunnel in rabbits [2,3].

Anterior cruciate ligament (ACL) reconstruction using a hamstring tendon graft is one of the most common procedures performed to treat ACL injury [5,6]. Both bone tunnels after ACL reconstruction with soft tissue grafts frequently become enlarged

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https://doi.org/10.1016/j.otsr.2019.01.005
1877-0568/

[7–9]. Although bone tunnel enlargement, especially on the femoral side, correlates with increased knee laxity in ACL reconstruction, it is controversial whether this tunnel enlargement affects the clinical outcomes [10–13]. However, an enlarged bone tunnel frequently leads to technical difficulties in creating new bone tunnels in revision surgery; hence, a two-stage procedure is sometimes required with bone grafting [14].

Bone tunnel enlargement at the aperture is increased by graft-tunnel motion and/or synovial fluid leakage within the bone tunnel [15–17]. Moreover, ACL reconstruction in both animals and humans results in fibrous bonding between the soft tissue graft and bone [18–20]. The mechanical properties of knees after ACL reconstruction with fibrous bonding between the soft tissue graft and bone tunnel are reportedly inferior to those after ACL reconstruction using the CaP-hybridized tendon graft in goats [21,22]. We considered that improvement of tendon-to-bone healing using the CaP-hybridized tendon could potentially prevent bone tunnel enlargement.

In a previous clinical trial, computed tomography (CT) revealed that the bone tunnel enlargement on the femoral side at 1 year after anatomic single-bundle ACL reconstruction was reduced in patients with the CaP-hybridized tendon graft compared with the untreated tendon graft due to anterior shift of the posterior wall and reduction of distal shift in the femoral bone tunnel [23]. However, this previous trial included bilateral ACL reconstruction cases, and the follow-up period was only 1 year. Therefore, the objective of the present study was to evaluate the progression of morphological changes in both bone tunnels after unilateral anatomic single-bundle ACL reconstruction using a CaP-hybridized tendon graft compared with that using an untreated tendon graft during 2 years of follow-up. We hypothesized that the CaP-hybridized tendon graft would prevent the progression of bone tunnel enlargement compared with the untreated tendon graft.

2. Patients and methods

2.1. Patients

Between July 2011 and December 2015, 90 patients who were scheduled to undergo arthroscopically-assisted unilateral anatomic single-bundle ACL reconstruction using a hamstring tendon graft were prospectively enrolled. The patients were randomly assigned to undergo the CaP method ($n = 45$), or the conventional method ($n = 45$). We only included patients who underwent three computed tomography (CT) analyses (at postoperative 1 week, 1 year, and 2 years) to analyze the progression of bone tunnel enlargement. Therefore, there was a final total of 19 patients in the CaP group, and 18 in the conventional group. The study was approved by the ethics committee of Ichihara Hospital (approval number: 1101). Informed consent was obtained from all enrolled patients. We excluded revision cases, multi-ligamentous surgery cases, and bilateral ACL reconstruction cases. All ACL reconstructions were performed by two experienced surgeons (T.K. and H.M.). The background characteristics did not differ between the two groups (Table 1). Moreover, there was no significant difference between the two groups regarding side-to-side difference, pivot-shift test results, Tegner scale [24], International Knee Documentation Committee knee examination results [25], and Lysholm knee scale [24] at each timepoint (Table 2). There was no case of rerupture or reoperation in either groups during follow-up. In the CaP group, there was no adverse event such as rerupture, infection, arthritis, or ossification into the intraarticular part of the graft. There was no

Table 1
Characteristics of the patients who underwent anatomic single-bundle anterior cruciate ligament reconstruction.

	CaP group ($n = 19$)	Conventional group ($n = 18$)	p-value
Age (years)	30.5 ± 12.2	25.1 ± 13.7	0.211
Sex (males/females)	9/10	11/7	0.238
Height (cm)	166.6 ± 6.7	170.0 ± 8.0	0.172
Weight (kg)	63.5 ± 10.8	64.8 ± 10.9	0.705
Duration from injury to operation (months)	11.6 ± 28.3	2.3 ± 1.9	0.176

Results are presented as the mean ± SD. CaP group: patients in whom a calcium phosphate-hybridized tendon graft was used; conventional group: patients in whom an untreated tendon graft was used.

Table 2
Clinical results after anatomic single-bundle anterior cruciate ligament reconstruction.

	CaP group ($n = 19$)	Conventional group ($n = 18$)	p-value
Side-to-side difference (mm)			
Preoperative	9.2 ± 3.9 ($n = 19$)	9.8 ± 2.4 ($n = 18$)	0.563
Postoperative 1 year	0.8 ± 1.3 ($n = 19$)	0.6 ± 1.1 ($n = 18$)	0.704
Postoperative 2 years	1.0 ± 1.6 ($n = 12$)	0.1 ± 0.9 ($n = 13$)	0.072
Pivot-shift test: 0, 1+, 2+, 3+ (n)			
Preoperative	0, 5, 14, 0 ($n = 19$)	0, 2, 16, 0 ($n = 18$)	0.238
Postoperative 1 year	18, 0, 1, 0 ($n = 19$)	17, 1, 0, 0 ($n = 18$)	0.367
Postoperative 2 years	16, 0, 0, 0 ($n = 16$)	14, 0, 0, 0 ($n = 14$)	–
IKDC objective grade: A, B, C, D (n)			
Preoperative	0, 2, 10, 7 ($n = 19$)	0, 0, 12, 6 ($n = 18$)	0.327
1 year	17, 1, 1, 0 ($n = 19$)	16, 2, 0, 0 ($n = 18$)	0.512
2years	14, 2, 0, 0 ($n = 16$)	14, 0, 0, 0 ($n = 14$)	0.171
Lysholm scale (points)			
Preoperative	54.1 ± 8.2 ($n = 19$)	51.0 ± 8.5 ($n = 18$)	0.274
Postoperative 1 year	98.4 ± 2.2 ($n = 19$)	98.1 ± 2.6 ($n = 18$)	0.348
Postoperative 2 years	98.7 ± 3.1 ($n = 19$)	99.9 ± 0.5 ($n = 17$)	0.110
Tegner scale: 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 (n)			
Preoperative (Preinjury)	0, 0, 0, 2, 1, 2, 10, 2, 0, 2, 0 ($n = 19$)	0, 0, 0, 0, 1, 0, 4, 7, 1, 5, 0 ($n = 18$)	0.071
Postoperative 1 year	0, 0, 0, 2, 4, 4, 6, 2, 0, 1, 0 ($n = 19$)	0, 0, 0, 0, 2, 4, 8, 2, 0, 2, 0 ($n = 18$)	0.660
Postoperative 2 years	0, 0, 0, 2, 1, 2, 9, 3, 0, 2, 0 ($n = 19$)	0, 0, 0, 0, 1, 2, 6, 5, 0, 3, 0 ($n = 17$)	0.670

Results are presented as the mean ± SD. IKDC: International Knee Documentation Committee; CaP group: patients in whom a calcium phosphate-hybridized tendon graft was used; conventional group: patients in whom an untreated tendon graft was used.

positive correlation between bone tunnel enlargement and clinical outcomes regarding knee instability in either group.

3. Methods

3.1.1. Surgical procedure and postoperative rehabilitation

The surgical procedure and postoperative rehabilitation were similar to our previous report [23]. Briefly, multi-stranded grafts were composed of either the semitendinosus tendon alone (16 knees in the CaP group, and 13 in the conventional group) or both the semitendinosus and gracilis tendons (three knees in the CaP group, and five in the conventional group); the harvested tendons used to create the graft did not significantly differ between the two groups. The tendon graft was hooked to the TightRope RT® (Arthrex, Naples, FL, USA) on the femoral side. The free ends were whipstitched with FiberWire® #2 (Arthrex) on the tibial side. The length and diameter of the tendon grafts were 50–70 mm and 6.5–10.0 mm, respectively. Both the femoral and tibial bone tunnels were anatomically created at the tibial and femoral insertions of the ACL. A 10- to 15-mm long femoral socket was created. The graft was fixed on the lateral femoral cortex, and then fixed to a screw and washer on the tibial side with an initial tension of 10 N using a tension meter at 20° of knee flexion.

At 1 week postoperatively, range of motion exercise and partial weight-bearing were started. Full weight-bearing walking was allowed at 3 weeks postoperatively. Running was allowed after 3 months, and return to sports after 6–12 months.

3.1.2. Intraoperative calcium phosphate hybridization method

The intraoperative CaP hybridization method was similar to our previous report [23]. After graft preparation, the intraarticular portion of the tendon graft was covered with the sleeve of a rubber glove tied on each side with nonabsorbable sutures to prevent hybridizing the CaP [23]. The length of the implanted tendon graft inserting in the femoral bone tunnel could be measured accurately. However, the length of the intraarticular portion and the tibial portion could not be measured accurately due to the characteristics of the surgical technique. Therefore, the intraarticular portion was uniformly 3 cm, and the remaining length was the tibial portion. The tendon graft was soaked in a calcium solution (100 mM $CaCl_2$ + 30 mM L-histidine, pH 7.4, 280 mOsm/l, 20 °C) for 30 s. The grafts were subsequently soaked in a $NaHPO_4$ solution (116.4 mM NaH_2PO_4:128.7 mM $Na_2HPO_4 \cdot 12H_2O$ = 15%:85%, pH 7.4, 280 mOsm/l, 20 °C) for 30 s. Before each soaking, the grafts were washed in a saline solution. This cycle was repeated 10 times [23].

3.2. Methods of assessment

All patients underwent CT evaluation at postoperative 1 week, 1 year, and 2 years. The full evaluation was performed independently by a radiologist who was blinded to the study grouping. CT scans (voltage 80 kV; Activion 16; Toshiba Medical Systems, Otawara, Japan) were performed with the knee in full extension to assess the femoral and tibial bone tunnels. Initial volume acquisition was performed with 2-mm cuts from 10 cm above the femoral tunnel to 10 cm below the tibial tunnel. Three-dimensional images were reconstructed using a Virtual Place Lexus workstation (AZE, Tokyo, Japan) [23,26]. As the joint aperture site of bone tunnels is reportedly enlarged after ACL reconstruction [27–29], we evaluated both the femoral and the tibial tunnels at the aperture. The tunnels were cut along planes perpendicular to the long axes.

In the bone tunnel enlargement evaluation, the tunnel enlargement rates of the cross-sectional area (CSA), anterior-posterior (AP) diameter (APD), and proximal-distal (PD) diameter (PDD) of the femoral bone tunnel at the apertures were calculated, and the CSA, APD, and medial-lateral (ML) diameter (MLD) of the tibial tunnels at the apertures were calculated [23,26]. The increase in tunnel CSA was calculated as: CSA increase rate (%) = (CSA at postoperative 1 week, 1 year, or 2 years–CSA of the drill) × 100/CSA of the drill. The increase in tunnel diameter was calculated as: tunnel diameter increase rate (%) = ((APD or PDD or MLD at postoperative 1 week, 1 year, or 2 years) – (APD or PDD or MLD of the drill)) × 100/APD or PDD or MLD of the drill [23,26]. The tunnel enlargement rates were compared between the two groups at each timepoint, and between each timepoint within the same group. In our previous report, bone tunnel enlargement rate was calculated relative to the bone tunnel size at 1 week postoperatively [23]. However, as bone tunnel enlargement has reportedly already appeared at 1 week postoperatively [16,17], the bone tunnel enlargement rate was calculated relative to the CSA and diameter of the intraoperative drill [26].

To evaluate the locations of the tunnel walls, we measured the locations of both the femoral and tibial tunnel walls at the aperture as percentages, using an anatomical coordinate system that included AP and PD axes for the femur, and AP and ML (medial-lateral) axes for the tibia [23,30,31]. On the femoral side, the distance from the posterior border of the medial wall of the femoral lateral condyle to the most anterior point of the notch was defined as 100% for the AP measurement, and the distance from the proximal border of the notch to the distal point of the notch roof was defined as 100% for the PD measurement. The tunnel wall positions in the AP and PD directions were calculated as percentages of these distances (Fig. 1). In the tibial bone tunnel, the distance from the anterior border to the posterior border of the tibial condyle was defined as 100% for the AP measurement, and the distance from the medial border of the tibial condyle to the lateral border of the tibia was defined as 100% for the ML measurement. The tunnel wall positions in the AP and ML directions were calculated as percentages of these distances (Fig. 2). The locations of the femoral and tibial bone tunnel walls were compared between the two groups

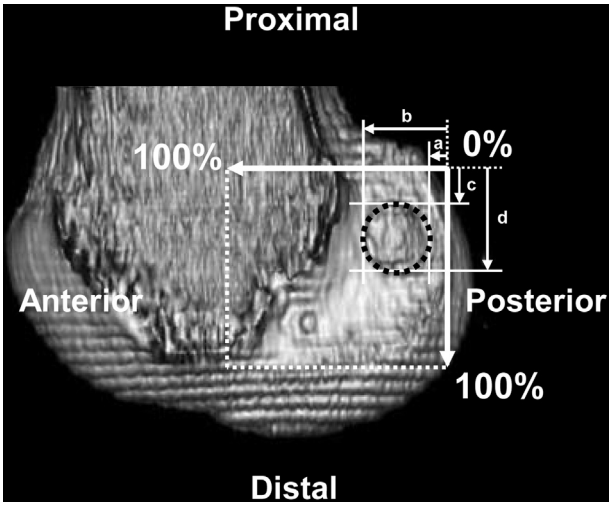

Fig. 1. Computed tomography image of the distal femur showing the measurement of the location of the femoral tunnel walls using the anatomical coordinate system [23,30,31]. The black dashed line indicates the femoral bone tunnel. The distance from the posterior border of the medial wall of the femoral lateral condyle to the most anterior point of the notch was defined as 100% for the anterior–posterior measurement, while the distance from the proximal border of the notch to the distal point of the notch roof was defined as 100% for the proximal–distal measurement. (a), (b), (c) and (d) are the positions of posterior, anterior, proximal and distal tunnel walls, respectively. The tunnel wall positions in the anterior–posterior and proximal–distal directions were calculated as percentages of these distances.

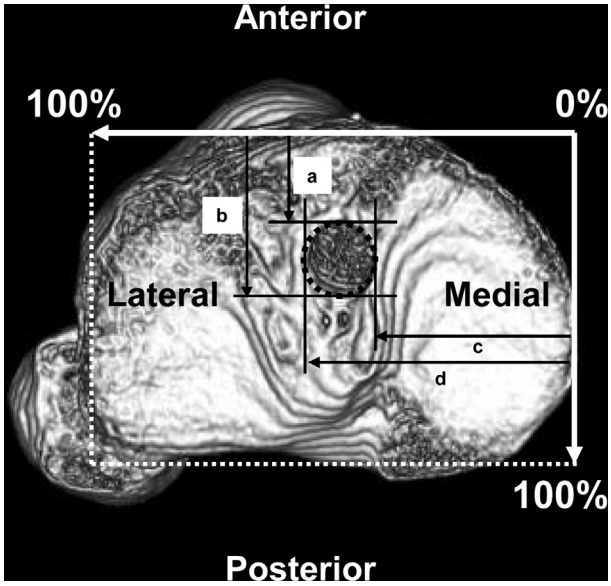

Fig. 2. Computed tomography image of the proximal tibia showing the measurement of the location of the tibial tunnel walls using the anatomical coordinate system [23,30,31]. The black dashed line indicates the tibial bone tunnel. The distance from the anterior border to the posterior border of the tibial condyle was defined as 100% for the anterior–posterior measurement, while the distance from the medial border of the tibial condyle to the lateral border of the tibia was defined as 100% for the medial–lateral measurement. (a), (b), (c) and (d) are the positions of anterior, posterior, medial and lateral tunnel walls, respectively. The tunnel wall positions in the anterior–posterior and medial–lateral directions were calculated as percentages of these distances.

at each timepoint, and between each timepoint within the same group.

The intra-class correlation coefficient (ICC) of the intra-rater reliability on the bone tunnel enlargement evaluation was 0.93–0.95, and inter-rater reliability on the bone tunnel enlargement evaluation was 0.92–0.97. The ICC of the intra-rater reliability on the evaluation of the morphological changes of the bone tunnels was 0.98–0.99, and inter-rater reliability on the evaluation of the morphological changes of the bone tunnels was 0.98–0.99. The measurement accuracy was very high.

3.3. Statistical analysis

The Student's t-test was used to analyze the results of the CT analyses between each group at the same timepoint. Repeated analysis of variance was used to analyze the results of the CT analyses between each timepoint within the same group. Significance was determined at $p < 0.05$.

4. Results

The bone tunnel enlargement results are summarized in Table 3. On the femoral side in the CaP group (Fig. 3A–C), there were no significant differences between timepoints in the CSA, APD, and PDD. On the femoral side in the conventional group (Fig. 3D–F), the CSA, APD, and PDD at 2 years postoperatively were smaller than the respective values at 1 year postoperatively. However, the CSA, APD, and PDD at 1 and 2 years postoperatively were larger than the respective values at 1 week postoperatively. The rates of increase of the CSA and PDD on the femoral side in the CaP group were significantly smaller than those in the conventional group at 1 year postoperatively.

On the tibial side in the CaP group (Fig. 4A–C), although the CSA and MLD at 1 year postoperatively were larger than the respective values at 1 week postoperatively, the CAS, APD, and MLD at 2 years postoperatively were smaller than the respective values at 1 year postoperatively. On the tibial side in the conventional group (Fig. 4D–F), the CAS and APD at 1 year postoperatively were larger than the respective values at 1 week postoperatively. However, the CAS and APD on the tibial side in the conventional group did not significantly differ between 1 and 2 years postoperatively. The MLD in the conventional group at 2 years postoperatively was smaller than that at 1 year postoperatively.

The locations of the tunnel walls are summarized in Table 4. On the femoral side in the CaP group (Fig. 3A–C), the posterior wall

Table 3
Bone tunnel enlargement after anatomic single-bundle anterior cruciate ligament reconstruction.

	Postoperative duration	CaP group	*p*-value for comparisons within the same group		Partial η^2/power	Conventional group	*p*-value for comparisons within the same group		Partial η^2/power	*p*-value for CaP group vs conventional group	Cohen's *d*
Femoral side											
CSA (%)	1 week	−9.3 ± 17.2	1 w vs 1 y	0.166	0.069/0.268	−12.6 ± 16.5	1 w vs 1 y	0.001**	0.466/0.977	0.557	0.195
	1 year	7.3 ± 43.2	1 w vs 2 y	0.316		49.7 ± 61.3	1 w vs 2 y	0.004**		0.020*	0.812
	2 years	3.5 ± 50.4	1 y vs 2 y	0.619		29.5 ± 52.3	1 y vs 2 y	0.003**		0.133	0.505
APD (%)	1 week	−0.4 ± 12.4	1 w vs 1 y	0.657	0.009/0.074	−5.6 ± 11.6	1 w vs 1 y	0.001**	0.413/0.957	0.191	0.439
	1 year	3.2 ± 33.2	1 w vs 2 y	0.962		19.2 ± 21.0	1 w vs 2 y	0.031**		0.091	0.589
	2 years	−0.8 ± 36.1	1 y vs 2 y	0.524		8.4 ± 19.5	1 y vs 2 y	0.001**		0.346	0.330
PDD (%)	1 week	−9.4 ± 11.8	1 w vs 1 y	0.070	0.088/0.339	−12.8 ± 14.8	1 w vs 1 y	0.001**	0.405/0.935	0.445	0.255
	1 year	0.7 ± 17.0	1 w vs 2 y	0.469		19.4 ± 35.4	1 w vs 2 y	0.014**		0.046*	0.713
	2 years	−4.7 ± 23.9	1 y vs 2 y	0.247		7.9 ± 28.0	1 y vs 2 y	0.002**		0.151	0.484
Tibial side											
CSA (%)	1 week	4.4 ± 8.4	1 w vs 1 y	0.010**	0.198/0.629	6.0 ± 12.6	1 w vs 1 y	0.044**	0.142/0.517	0.644	0.155
	1 year	23.9 ± 31.2	1 w vs 2 y	0.329		18.7 ± 23.0	1 w vs 2 y	0.643		0.573	0.190
	2 years	12.4 ± 35.3	1 y vs 2 y	0.019**		8.6 ± 24.2	1 y vs 2 y	0.086		0.708	0.127
APD (%)	1 week	2.6 ± 4.8	1 w vs 1 y	0.012	0.196/0.720	5.6 ± 7.3	1 w vs 1 y	0.009**	0.177/0.635	0.139	0.506
	1 year	14.7 ± 19.0	1 w vs 2 y	0.654		14.7 ± 14.1	1 w vs 2 y	0.629		0.994	0.003
	2 years	5.0 ± 22.8	1 y vs 2 y	0.007**		7.6 ± 15.9	1 y vs 2 y	0.059		0.691	0.135
MLD (%)	1 week	1.7 ± 4.6	1 w vs 1 y	0.039**	0.203/0.743	2.2 ± 4.4	1 w vs 1 y	0.208	0.100/0.365	0.709	0.124
	1 year	11.8 ± 18.9	1 w vs 2 y	0.912		7.6 ± 15.7	1 w vs 2 y	0.698		0.466	0.244
	2 years	2.1 ± 18.6	1 y vs 2 y	0.005**		0.7 ± 14.8	1 y vs 2 y	0.040**		0.791	0.089

Results are presented as the mean ± SD. CSA: cross-sectional area; APD: anterior-posterior diameter; PDD: proximal-distal diameter; MLD: medial-lateral diameter; CaP group: patients in whom a calcium phosphate-hybridized tendon graft was used ($n = 19$); Conventional group: patients in whom an untreated tendon graft was used ($n = 18$).

* $p < 0.05$: significant difference between the two groups.

** $p < 0.05$ compared within the same group.

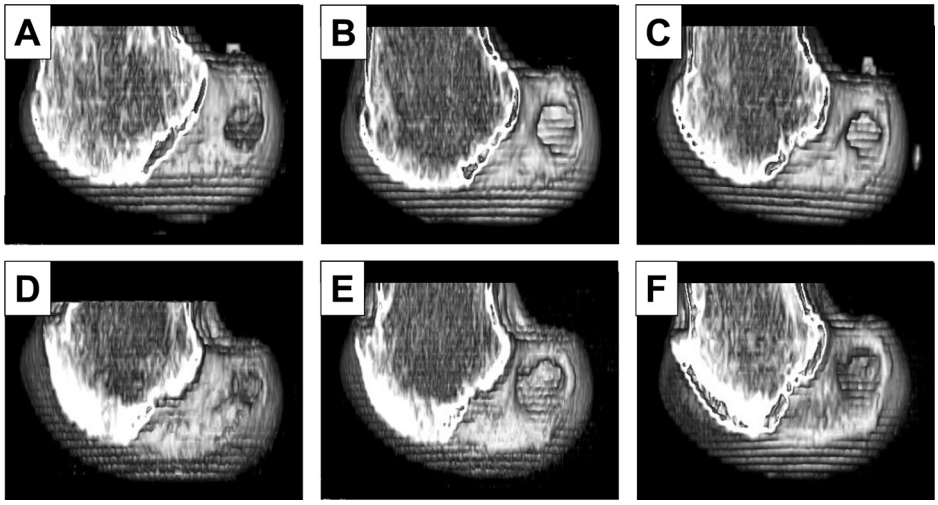

Fig. 3. Computed tomography images of femoral tunnel in the CaP group (A, 1 week; B, 1 year; C, 2 years) and conventional group (D, 1 week; E, 1 year; F, 2 years). The CaP group shows no progression of bone tunnel enlargement during 2 years of follow-up. Both the anterior and posterior walls of the bone tunnel in the CaP group only shift anteriorly during 2 years of follow-up. The conventional group shows progression of bone tunnel enlargement during 2 years of follow-up. In the conventional group, the proximal wall of the bone tunnel shifts proximally, and the distal wall shifts distally.

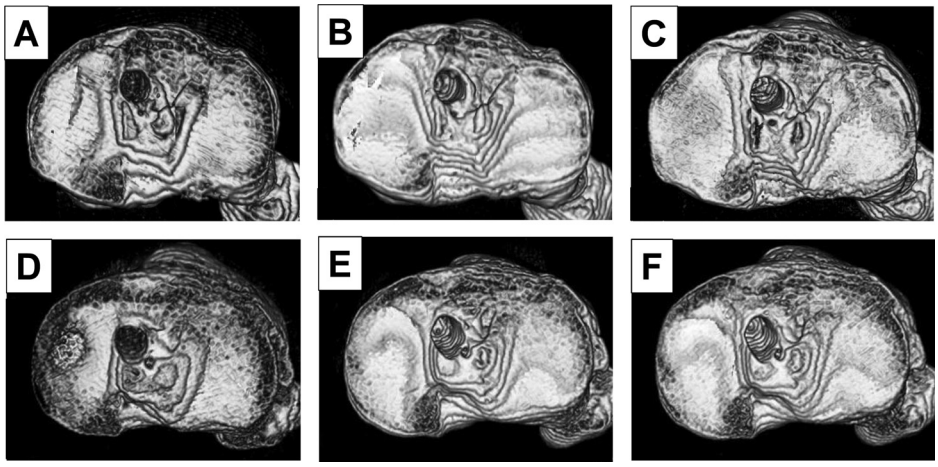

Fig. 4. Computed tomography images of tibial tunnel in the CaP group (A, 1 week; B, 1 year; C, 2 years) and conventional group (D, 1 week; E, 1 year; F, 2 years). The CaP group shows no progression of bone tunnel enlargement during 2 years of follow-up. In the conventional group, the anterior-posterior diameter of the bone tunnel is enlarged at 1 year, and the enlargement is maintained for 2 years.

was shifted anteriorly at 1 year postoperatively compared with 1 week postoperatively. On the femoral side in the conventional group (Fig. 3D–F), the posterior wall was shifted anteriorly at 2 years postoperatively compared with 1 week and 1 year postoperatively. This indicates that the anterior translation of the posterior wall of the femoral tunnel in the CaP group occurred more rapidly than that in the conventional group. In the conventional group, the distal wall of the femoral tunnel was shifted distally at 1 and 2 years postoperatively compared with 1 week postoperatively. Moreover, in the conventional group, the proximal wall of the femoral tunnel was shifted proximally at 1 year postoperatively compared with 1 week postoperatively. In both groups, the anterior walls of the femoral tunnel shifted anteriorly at 1 and 2 years postoperatively compared with 1 week postoperatively.

On the tibial side in the CaP group (Fig. 4–C), the anterior wall was shifted posteriorly at 2 years postoperatively compared with 1 year postoperatively; furthermore, the medial wall of the tibial tunnel was shifted laterally at 2 years postoperatively compared with 1 week and 1 year postoperatively, and the lateral wall was shifted laterally at 1 and 2 years postoperatively compared with 1 week postoperatively. In the conventional group (Fig. 4D–F), the medial wall of the tibial tunnel was shifted laterally at 1 and 2 years postoperatively compared with 1 week postoperatively, and the lateral wall was shifted laterally at 1 year postoperatively compared with 1 week postoperatively. The lateral wall of the tibial tunnel in the CaP group at 2 years postoperatively was more located more laterally than that in the conventional group.

5. Discussion

The CaP group showed no progression of femoral bone tunnel enlargement as assessed by the CSA, APD, and PDD during 2 years of follow-up. Both the anterior and posterior walls of the femoral bone tunnel in the CaP group had shifted anteriorly at 1 year postoperatively, indicating that the femoral bone tunnel did not expand, but only shifted anteriorly during 2 years of follow-up. In contrast, although the bone tunnels in the conventional group as assessed by the CSA, APD, and PDD were smaller at 2 years postoperatively than at 1 year postoperatively, the CSA, APD, and PDD were enlarged at 1 and 2 years postoperatively compared with 1 week postoperatively. The anterior wall of the femoral bone tunnel in the conventional group was shifted anteriorly at

Table 4
Locations of the tunnel walls after anatomic single-bundle anterior cruciate ligament reconstruction.

	Postoperative duration	CaP group	*p* value for comparisons within the same group		Partial η^2/power	Conventional group	*p*-value for comparisons within the same group		Partial η^2/power	*p*-value for the CaP group vs the conventional group	Cohen's *d*
Femoral side											
Anterior wall (%)	1 week	36.2 ± 7.0	1 w vs 1 y	<0.001**	0.589/1.000	33.3 ± 7.3	1 w vs 1 y	<0.001**	0.628/1.000	0.225	0.406
	1 year	45.4 ± 7.9	1 w vs 2 y	<0.001**		45.6 ± 7.5	1 w vs 2 y	<0.001**		0.941	0.025
	2 years	45.2 ± 9.1	1 y vs 2 y	0.836		44.5 ± 11.4	1 y vs 2 y	0.451		0.836	0.069
Posterior wall (%)	1 week	10.0 ± 5.0	1 w vs 1 y	0.010**	0.194/0.715	10.3 ± 6.6	1 w vs 1 y	0.145	0.246/0.682	0.860	0.059
	1 year	15.0 ± 8.1	1 w vs 2 y	0.073		11.8 ± 4.9	1 w vs 2 y	0.023**		0.157	0.493
	2 years	14.0 ± 8.8	1 y vs 2 y	0.503		15.1 ± 7.0	1 y vs 2 y	0.028**		0.674	0.141
Proximal wall (%)	1 week	23.7 ± 10.8	1 w vs 1 y	0.877	0.030/0.136	27.0 ± 12.1	1 w vs 1 y	0.018**	0.081/0.250	0.399	0.281
	1 year	24.0 ± 10.0	1 w vs 2 y	0.429		23.9 ± 10.0	1 w vs 2 y	0.399		0.963	0.016
	2 years	22.2 ± 8.8	1 y vs 2 y	0.340		25.0 ± 11.6	1 y vs 2 y	0.537		0.412	0.275
Distal wall (%)	1 week	55.6 ± 17.5	1 w vs 1 y	0.728	0.005/0.063	54.8 ± 12.3	1 w vs 1 y	0.004**	0.328/0.947	0.875	0.053
	1 year	56.9 ± 17.3	1 w vs 2 y	0.806		65.2 ± 14.2	1 w vs 2 y	0.006**		0.121	0.527
	2 years	56.4 ± 14.5	1 y vs 2 y	0.812		65.1 ± 15.2	1 y vs 2 y	0.939		0.084	0.585
Tibial side											
Anterior wall (%)	1 week	25.1 ± 5.9	1 w vs 1 y	0.310	0.140/0.535	24.1 ± 4.9	1 w vs 1 y	0.665	0.103/0.376	0.562	0.194
	1 year	24.1 ± 4.9	1 w vs 2 y	0.203		24.4 ± 5.1	1 w vs 2 y	0.078		0.863	0.057
	2 years	26.6 ± 6.0	1 y vs 2 y	0.024**		25.3 ± 5.7	1 y vs 2 y	0.140		0.485	0.232
Posterior wall (%)	1 week	43.3 ± 4.9	1 w vs 1 y	0.382	0.046/0.164	42.5 ± 5.8	1 w vs 1 y	0.197	0.172/0.526	0.638	0.156
	1 year	44.0 ± 6.0	1 w vs 2 y	0.302		43.5 ± 5.1	1 w vs 2 y	0.051		0.798	0.085
	2 years	44.8 ± 7.6	1 y vs 2 y	0.491		45.0 ± 6.9	1 y vs 2 y	0.088		0.935	0.027
Medial wall (%)	1 week	38.7 ± 3.9	1 w vs 1 y	0.456	0.203/0.743	37.3 ± 3.6	1 w vs 1 y	<0.001**	0.323/0.843	0.290	0.354
	1 year	39.2 ± 3.2	1 w vs 2 y	0.016**		40.1 ± 2.5	1 w vs 2 y	0.012**		0.320	0.336
	2 years	40.5 ± 3.5	1 y vs 2 y	0.017**		40.2 ± 4.5	1 y vs 2 y	0.901		0.852	0.062
Lateral wall (%)	1 week	51.3 ± 3.7	1 w vs 1 y	0.030**	0.228/0.805	49.6 ± 4.3	1 w vs 1 y	0.001**	0.202/0.573	0.207	0.423
	1 year	52.7 ± 3.0	1 w vs 2 y	0.011**		51.7 ± 3.3	1 w vs 2 y	0.370		0.327	0.327
	2 years	53.0 ± 3.6	1 y vs 2 y	0.626		50.5 ± 3.2	1 y vs 2 y	0.077		0.033*	0.731

Results are presented as the mean ± SD. CaP group: patients in whom a calcium phosphate-hybridized tendon graft was used ($n = 19$); Conventional group: patients in whom an untreated tendon graft was used ($n = 18$).

* $p < 0.05$: significant difference between the two groups.

** $p < 0.05$ compared within the same group.

1 year postoperatively, similarly to the CaP group. However, the anterior shift of the posterior wall of the femoral bone tunnel in the conventional group at 2 years postoperatively was less than that in the CaP group. Moreover, the proximal wall of the femoral bone tunnel in the conventional group was shifted proximally at 1 year postoperatively, while the distal wall was shifted distally at 1 and 2 years postoperatively. The CSA and PDD of the femoral bone tunnel were larger in the conventional group than in the CaP group at 1 year postoperatively, similarly to a previous report [23]. Therefore, the femoral bone tunnel in the conventional group expanded vertically and shifted anteriorly during 2 years of follow-up. A previous study reported that the maximum contact pressure of the graft at the anterior portion of the femoral tunnel occurred when the knee was in full extension [32]. Moreover, the femoral tunnel aperture reportedly translates anteriorly and distally with time after ACL reconstruction [28]. Our results in the conventional group supported these previous reports. These morphological changes in the CaP group in which the femoral bone tunnel underwent less enlargement distally and proximally compared with the conventional group indicate reduced femoral bone tunnel enlargement. As the CaP-hybridized tendon graft enhances bone formation on the tendon surface in the bone tunnel [2–4], this osteogenic effect can form new bone in the posterior, distal, and proximal walls of the femoral tunnel. Hence, the promotion of new bone formation by the CaP-hybridized tendon graft effectively reduces femoral bone tunnel enlargement in anatomic single-bundle ACL reconstruction compared with the untreated tendon graft.

In the CaP group, although the CSA and MLD of the tibial bone tunnel were enlarged at 1 year postoperatively, the CSA, APD, and MLD reduced during 2 years of follow-up. In the conventional group, although the MLD of the tibial bone tunnel at 2 years postoperatively was smaller than that at 1 year postoperatively, the CSA and APD were enlarged at 1 year postoperatively, and this enlargement of the bone tunnel was maintained for 2 years postoperatively. A previous study reported that tibial bone tunnel enlargement frequently occurs at the posterior portion [33]; our results in the conventional group supported these previous findings. The posterior shift of the anterior wall of the tibial bone tunnel in the CaP group at 2 years postoperatively was considered to be due to the osteogenic effect of the CaP-hybridized graft. The tibial bone tunnel in the CaP group underwent a smaller amount of anterior shift, and showed enlargement and then reduction compared with the conventional group, which suggests reduced tibial bone tunnel enlargement. Although the medial wall of the tibial bone tunnel shifted laterally in both groups, the shift of the lateral wall of the tibial bone tunnel progressed in the CaP group, and the lateral wall of the tibial bone tunnel in the CaP group at 2 years postoperatively was located more laterally than that in the conventional group. Unlike the femoral side, the implanted part of the graft to be inserted into the tibial bone tunnel could not be accurately measured, and so the CaP-hybridization might have been insufficient.

Bone tunnel enlargement at the aperture is reported in conventional ACL reconstruction, particularly on the femoral side [10], and this is associated with graft-tunnel motion comprising both longitudinal micromotion (bungee effect) and transverse micromotion (windshield wiper effect) [16,17,34]; furthermore, synovial fluid cytokines caused delayed tendon-to-bone healing at the tunnel aperture [15]. In the early phase after ACL reconstruction, the tendon-bone interface may be subjected to stress before biologic incorporation is complete. The CaP-hybridized tendon graft is reportedly directly bonded with the bone tunnel at 2 to 3 weeks postoperatively in rabbits [2,3], and there is enhanced tendon-to-bone healing in the cartilage layer and newly formed bone at the

femoral and tibial tunnel aperture in ACL reconstruction in goats [21,22]. The new bone formation in the early phase and the cartilage layer formation can act as a shock absorber against graft-tunnel motion and protect against synovial fluid. Bone tunnel enlargement can also be caused by tunnel malpositioning [13]. In the present study, there was no significant difference between the two groups in the locations of the walls of both bone tunnels at 1 week postoperatively, indicating that the immediately postoperative tibial and femoral bone tunnel positions can be equivalent in both groups.

The present study had some limitations. The evaluations were only performed at three timepoints, the follow-up period was short (2 years), and the number of evaluated patients in each group was small compared with the total number assigned to each group (19/45 in the CaP group, and 18/45 in the conventional group). Studies with longer follow-up, a complete dataset, and multiple evaluation timepoints are needed to further investigate the morphological changes in the bone tunnels and the timing of these changes. Moreover, investigation with longer follow-up and sufficient samples into the relationship between bone tunnel enlargement and clinical results is necessary.

6. Conclusions

In anatomic single-bundle ACL reconstruction, the femoral bone tunnel in the CaP group did not expand or progress with time compared with the conventional group, while the tibial bone tunnel in the CaP group expanded for up to 1 year postoperatively and then reduced for up to 2 years postoperatively. The CaP-hybridized tendon can prevent the progression of bone tunnel enlargement.

Disclosure of interest

The authors declare that they have no competing interest.

Funding source

This work was supported by the Japan Sports Medicine Foundation, 2015.

Authors' contributions

H.M.: Study design, main surgeon of the study, data collection, data analysis, writing and correction of the manuscript, submission.

T.K.: Main surgeon of the study, correction of the manuscript.

K.I.: Correction of the manuscript, supervision.

M.S.: Correction of the manuscript, supervision.

All authors read and approved the final submitted version of the manuscript.

Acknowledgments

We thank Kelly Zammit, BVSc, from Edanz Group (www.edanzediting.com/ac), for editing a draft of this manuscript.

References

[1] Taguchi T, Kishida A, Akashi M. Hydroxyapatite formation on/in hydrogels using a novel alternate soaking process. Chem Lett 1998;8:711–2.
[2] Mutsuzaki H, Sakane M, Nakajima H, Ito A, Hattori S, Miyanaga Y, et al. Calcium-phosphate-hybridized tendon directly promotes regeneration of tendon-bone insertion. J Biomed Mater Res A 2004;70A:319–27.
[3] Mutsuzaki H, Sakane M, Ito A, Nakajima H, Hattori S, Miyanaga Y, et al. The interaction between osteoclast-like cells and osteoblasts mediated by nanophase calcium phosphate-hybridized tendons. Biomaterials 2005;26:1027–34.
[4] Mutsuzaki H, Fujie H, Nakajima H, Fukagawa M, Nomura S, Sakane M. Comparison of postoperative biomechanical function between anatomic double-bundle and single-bundle ACL reconstructions using calcium phosphate-hybridized tendon grafts in goats. Orthop Traumatol Surg Res 2017;103:239–43.
[5] Poehling-Monaghan KL, Salem H, Ross KE, Secrist E, Ciccotti MC, Tjoumakaris F, et al. Long-term outcomes in anterior cruciate ligament reconstruction: a systematic review of patellar tendon versus hamstring autografts. Orthop J Sports Med 2017;5 [2325967117709735].
[6] Ciccotti MC, Secrist E, Tjoumakaris F, Ciccotti MG, Freedman KB. Anatomic anterior cruciate ligament reconstruction via independent tunnel drilling: a systematic review of randomized controlled trials comparing patellar tendon and hamstring autografts. Arthroscopy 2017;33 [1062–71.e5].
[7] Webster KE, Feller JA, Hameister KA. Bone tunnel enlargement following anterior cruciate ligament reconstruction: a randomised comparison of hamstring and patellar tendon grafts with 2-year follow-up. Knee Surg Sports Traumatol Arthrosc 2001;9:86–91.
[8] Iorio R, Vadalà A, Argento G, Di Sanzo V, Ferretti A. Bone tunnel enlargement after ACL reconstruction using autologous hamstring tendons: a CT study. Int Orthop 2007;31:49–55.
[9] Stolarz M, Ficek K, Binkowski M, Wróbel Z. Bone tunnel enlargement following hamstring anterior cruciate ligament reconstruction: a comprehensive review. Phys Sports Med 2017;45:31–40.
[10] Feller JA, Webster KE. A randomized comparison of patellar tendon and hamstring tendon anterior cruciate ligament reconstruction. Am J Sports Med 2003;31:564–73.
[11] Fauno P, Kaalund S. Tunnel widening after hamstring anterior cruciate ligament reconstruction is influenced by the type of graft fixation used: a prospective randomized study. Arthroscopy 2005;21:1337–41.
[12] Järvelä T, Moisala AS, Paakkala T, Paakkala A. Tunnel enlargement after double-bundle anterior cruciate ligament reconstruction: a prospective, randomized study. Arthroscopy 2008;24:1349–57.
[13] Xu Y, Ao Y, Wang J, Yu J, Cui G. Relation of tunnel enlargement and tunnel placement after single-bundle anterior cruciate ligament reconstruction. Arthroscopy 2011;27:923–32.
[14] Thomas NP, Kankate R, Wandless F, Pandit H. Revision anterior cruciate ligament reconstruction using a 2-stage technique with bone grafting of the tibial tunnel. Am J Sports Med 2005;33:1701–9.
[15] Berg EE, Pollard ME, Kang Q. Interarticular bone tunnel healing. Arthroscopy 2001;17:189–95.
[16] Rodeo SA, Kawamura S, Kim HJ, Dynybil C, Ying L. Tendon healing in a bone tunnel differs at the tunnel entrance versus the tunnel exit: an effect of graft-tunnel motion? Am J Sports Med 2006;34:1790–800.
[17] Rodeo SA, Kawamura S, Ma CB, Deng XH, Sussman PS, Hays P, et al. The effect of osteoclast activity on tendon-to-bone healing: an experimental study in rabbits. J Bone Joint Surg Am 2007;89:2250–9.
[18] Grana WA, Egle DM, Mahnken R, Goodhart CW. An analysis of autograft fixation after anterior cruciate ligament reconstruction in a rabbit model. Am J Sports Med 1994;22:344–51.
[19] Pinczewski LA, Clingeleffer AJ, Otto DD, Bonar SF, Corry IS. Integration of hamstring tendon graft with bone in reconstruction of the anterior cruciate ligament. Arthroscopy 1997;13:641–3.
[20] Nebelung W, Becker R, Urbach D, Röpke M, Roessner A. Histological findings of tendon-bone healing following anterior cruciate ligament reconstruction with hamstring grafts. Arch Orthop Trauma Surg 2003;123:158–63.
[21] Mutsuzaki H, Sakane M, Fujie H, Hattori S, Kobayashi H, Ochiai N. Effect of calcium phosphate–hybridized tendon graft on biomechanical behavior in anterior cruciate ligament reconstruction in a goat model: novel technique for improving tendon-bone healing. Am J Sports Med 2011;39:1059–66.
[22] Mutsuzaki H, Fujie H, Nakajima H, Fukagawa M, Nomura S, Sakane M. Effect of calcium phosphate hybridized tendon graft in anatomical single-bundle ACL reconstruction in goats. Orthop J Sports Med 2016;4 [2325967116662653].
[23] Mutsuzaki H, Kinugasa T, Ikeda K, Sakane M. Calcium phosphate-hybridized tendon grafts reduce femoral bone tunnel enlargement in anatomic single-bundle ACL reconstruction. Knee Surg Sports Traumatol Arthrosc 2018;26:500–7.
[24] Tegner Y, Lysholm J. Rating systems in the evaluation of knee ligament injuries. Clin Orthop Relat Res 1985;198:43–9.
[25] Hefti F, Muller W, Jakob RP, Staubli HU. Evaluation of knee ligament injuries with the IKDC form. Knee Surg Sports Traumatol Arthrosc 1993;1:226–34.
[26] Mutsuzaki H, Kanamori A, Ikeda K, Hioki S, Kinugasa T, Sakane M. Effect of calcium phosphate-hybridized tendon graft in anterior cruciate ligament reconstruction: a randomized controlled trial. Am J Sports Med 2012;40:1772–80.
[27] Araki D, Kuroda R, Matsumoto T, Nagamune K, Matsushita T, Hoshino Y, et al. Three-dimensional analysis of bone tunnel changes after anatomic double-bundle anterior cruciate ligament reconstruction using multidetector-row computed tomography. Am J Sports Med 2014;42:2234–41.
[28] Tachibana Y, Mae T, Shino K, Kanamoto T, Sugamoto K, Yoshikawa H, et al. Morphological changes in femoral tunnels after anatomic anterior cruciate ligament reconstruction. Knee Surg Sports Traumatol Arthrosc 2015;23:3591–600.
[29] Taketomi S, Inui H, Sanada T, Yamagami R, Tanaka S, Nakagawa T. Eccentric femoral tunnel widening in anatomic anterior cruciate ligament reconstruction. Arthroscopy 2014;30:701–9.
[30] Forsythe B, Kopf S, Wong AK, Martins CA, Anderst W, Tashman S, et al. The location of femoral and tibial tunnels in anatomic double-bundle anterior cruciate ligament reconstruction analyzed by three-dimensional computed tomography models. J Bone Joint Surg Am 2010;92:1418–26.
[31] Kopf S, Forsythe B, Wong AK, Tashman S, Anderst W, Irrgang JJ, et al. Nonanatomic tunnel position in traditional transtibial single-bundle anterior

cruciate ligament reconstruction evaluated by three-dimensional computed tomography. J Bone Joint Surg Am 2010;92:1427–31.
[32] Segawa H, Koga Y, Omori G, et al. Influence of the femoral tunnel location and angle on the contact pressure in the femoral tunnel in anterior cruciate ligament reconstruction. Am J Sports Med 2003;31:444–8.
[33] Nebelung W, Becker R, Merkel M, Röpke M. Bone tunnel enlargement after anterior cruciate ligament reconstruction with semitendinosus tendon using Endobutton fixation on the femoral side. Arthroscopy 1998;14:810–5.
[34] Paessler HH, Mastrokalos DS. Anterior cruciate ligament reconstruction using semitendinosus and gracilis tendons, bone patellar tendon, or quadriceps tendon-graft with press-fit fixation without hardware. A new and innovative procedure. Orthop Clin North Am 2003;34:49–64.