Osteoconductive Scaffold Placed at the Femoral Tunnel Aperture in Hamstring Tendon ACL Reconstruction

A Randomized Controlled Trial

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Background: Bone tunnel enlargement after single-bundle anterior cruciate ligament reconstruction remains an unsolved problem that complicates revision surgery.

Hypothesis: Positioning of an osteoconductive scaffold at the femoral tunnel aperture improves graft-to-bone incorporation and thereby decreases bone tunnel widening.

Study Design: Randomized controlled trial; Level of evidence, 1.

Methods: In a 1:1 ratio, 56 patients undergoing primary anterior cruciate ligament reconstruction were randomized to receive femoral fixation with cortical suspension fixation and secondary press-fit fixation at the tunnel aperture of the tendon graft only (control) or with augmentation by an osteoconductive scaffold (intervention). Adverse events, patient-reported outcomes, and passive knee stability were recorded over 2 years after the index surgery. Three-dimensional bone tunnel widening was assessed using computed tomography at the time of surgery and 4.5 months and 1 year postoperatively.

Results: The intervention group exhibited a similar number of adverse events as the control group (8 vs 10; $P = .775$) including 2 partial reruptures in both groups. The approach was feasible, although 1 case was encountered where the osteoconductive scaffold was malpositioned without adversely affecting the patient's recovery. There was no difference between the intervention and control groups in femoral bone tunnel enlargement, as expressed by the relative change in tunnel volume from surgery to 4.5 months (mean ± SD, 36% ± 25% vs 40% ± 25%; $P = .644$) and 1 year (19% ± 20% vs 17% ± 25%; $P = .698$).

Conclusion: Press-fit graft fixation with an osteoconductive scaffold positioned at the femoral tunnel aperture is safe but does not decrease femoral bone tunnel enlargement at postoperative 1 year.

Registration: NCT03462823 (ClinicalTrials.gov identifier).

Keywords: ACL reconstruction; hamstring tendons; press-fit; tunnel widening; osteoconduction; graft healing

All–soft tissue tendon grafts are a frequent choice for anterior cruciate ligament (ACL) reconstruction, and although clinical results are generally satisfactory, impaired graft-to-bone healing resulting in bone tunnel enlargement (BTE) is a frequent radiological finding.[1,4,7,36] Whereas BTE may not affect the functional outcome, it complicates revision surgery, often requiring a 2-staged surgical procedure with bone grafting and delayed ligament reconstruction. Its causes are multifactorial and include biological factors, such as osteolytic cytokines and poor bone quality,[8,38] as well as mechanical factors.[29] Improper fixation of the graft at the tunnel aperture and resulting graft motion during flexion-extension cycles of the knee leading to impaired graft incorporation are believed to be mechanical causes of BTE.[6,25]

To prevent graft micromotion, suspensory button or cross-pin fixation is often reinforced with an interference screw placed at the tunnel entrance. Other surgeons rely on press-fit placement of the graft in the femoral tunnel without additional secondary fixation.[17] Metal interference screws show adequate clinical performance but can be difficult to remove in case of revision surgery, and they distort magnetic resonance images.[23] Bioabsorbable interference screws, in contrast, carry the risk of breakage during

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insertion and may induce an inflammatory response, and some compounds may promote BTE themselves.[4,34] Regardless of the material of choice, interference screws add the risk of suture or graft laceration during insertion and have been linked with an increased risk for rerupture.[6,11,32]

To mitigate these limitations, surgical techniques using bone plugs as a secondary fixation have been proposed with promising results, functionally and with regard to BTE. In these studies, autologous bone obtained during impaction of the tibial tunnel[1,16,22] or xenogeneic bone material[18] was shaped into a conical cylinder and used in place of an interference screw. We have expanded on this concept in that we enlace an osteoconductive scaffold (OCS) into the tendon graft and achieve secondary fixation by press-fitting the construct into the femoral tunnel aperture.

In the current study, we assessed the approach of positioning an OCS at the femoral tunnel aperture during ACL reconstruction in terms of safety, technical feasibility in the operating room, functional outcomes, and BTE.

METHODS

Study Design and Patient Population

The study protocol was approved by the local ethics committee, and all patients provided informed consent. This randomized single-blind clinical trial included 56 patients, who were allocated into control and intervention groups at a ratio of 1:1. The study was powered a priori ($P = .8$) to detect a 20% difference in relative bone tunnel volume change between the groups at the 1-year follow-up, assuming an overall SD[3] of ±25.2% and anticipating a 10% patient dropout rate.[12] Patients aged between 18 and 60 years with a primary ACL rupture scheduled for surgical reconstruction were eligible for inclusion. Presurgical exclusion criteria were prior surgery of the index knee. Patients with extensive cartilage damage (Outerbridge grade >3),[28] multiligament damage with an indication for additional surgical intervention, and extensive meniscal resection as determined intraoperatively were excluded from the study. After final inclusion, each patient was randomly allocated into 1 of the 2 groups via sealed envelopes.

Surgical Procedure

ACL reconstruction was conducted according to the standard procedure in our hospital. A semitendinosus tendon autograft (combined with gracilis tendon if necessary) was harvested from the index knee with a tendon stripper. The tendon was folded twice to yield a 4-strand graft, and the graft ends were compacted with multiple suture nooses. In patients allocated to the intervention group, the OCS was inserted into the tendon graft. For the intra-articular procedure, standard medial and lateral parapatellar arthroscopy portals were used. After overdrilling with a 4.5-mm drill, the final femoral graft tunnel was created with a depth of 27 mm by a cannulated drill through the medial portal. The diameter of the drill for the femoral socket tunnel was 0.5 mm smaller than the tendon graft diameter to achieve press-fit. The tunnel diameter was slightly increased with a bone dilator where required. The tibial tunnel was prepared by using a drill guide (Karl Storz) targeted at the center of the tibial ACL footprint. The tendon graft was inserted into the femoral bone tunnel through the tibial tunnel. The graft was secured at the femoral tunnel with a flipping device on the cortical bone (Flipptack; Karl Storz). Tibial graft fixation was achieved via an interference screw (Megafix; Karl Storz) at the articular side and a suture button (Endotack; Karl Storz) at the tibial cortex. Surgical parameters were recorded, including additional procedures, autograft composition, and tunnel and graft diameters. Tunnel diameters were inferred per the drill diameter, and graft diameter was measured with a tendon thickness tester (Karl Storz).

Rehabilitation

Patients treated with an isolated ACL reconstruction were advised to load the affected leg with no more than half body weight for 3 weeks with free range of motion. In cases of ACL reconstruction with meniscal repair, maximum loading was set at 15 kg for 6 weeks, and range of motion was limited at 60° and 90° of knee flexion for the first 2 weeks and the following 2 weeks, respectively.

Osteoconductive Scaffold

The OCS used in the study is composed of a natural mineral matrix of bovine origin, reinforced with biodegradable synthetic polymers and natural collagen derivatives (BTB-Converter; ZuriMED Technologies).[9] During graft preparation, it was enlaced into the tendon graft to be positioned at the femoral tunnel aperture central between the tendon strands spanning the entirety of the tunnel diameter (Figure 1).

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Ethical approval for this study was obtained from the ethics commission of the Canton of Zurich (No. 2017-00750).

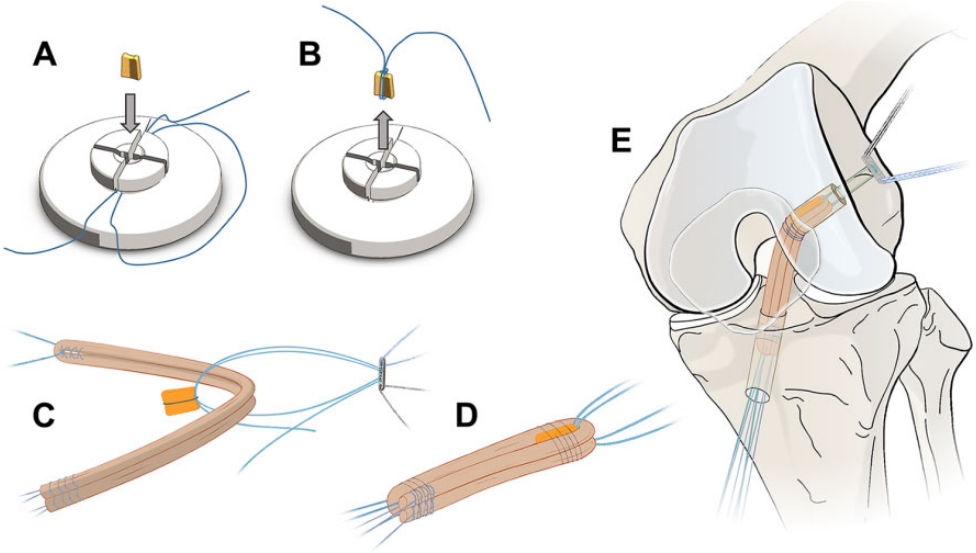

Figure 1. Experimental surgical procedure. The osteoconductive scaffold is (A, B) connected to the femoral suspension fixation loop and (C, D) enlaced into the tendon graft. (E) After graft insertion, the osteoconductive scaffold is positioned at the femoral tunnel aperture spanning the entirety of the tunnel diameter.

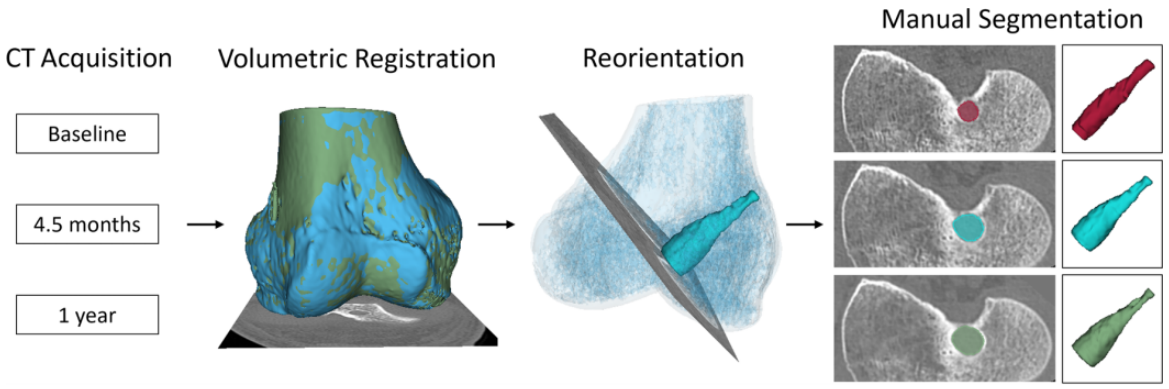

Figure 2. Workflow applied for the computation of the femoral and tibial bone tunnel volume. Registration of the volumes acquired at different time points ensures identical length of the segmentation and identical position and orientation of the bone tunnel aperture cross-sectional area. CT, computed tomography.

Adverse Events and Technical Feasibility

Any occurrences of adverse events were recorded over the study period. Adverse events were assessed with a potential relation to the surgical procedure or patient outcome. Technical feasibility was assessed by documenting any unforeseen technical difficulties related to the intervention. The duration of surgery was recorded to quantify the procedural burden on the workflow introduced by the addition of the intervention under study.

Assessment of Femoral and Tibial BTE

The size of the bone tunnel and the degree of tunnel enlargement were quantified by its entire volume (in cubic mm) at the different time points and its relative change thereof over time. As a secondary outcome parameter, we quantified the area of the tunnel aperture cross section (in mm^2). Computed tomography (CT) images were acquired at an isometric resolution of 0.5 mm. The reconstructed volume was first cropped to separate the femur and the tibia. The volumes of the 2 follow-up scans were then registered onto the baseline measurement (Demon registration[20]). The view was reoriented to be orthogonal to the bone tunnel. In each slice, the bone tunnel was segmented manually, starting from the articular side at the first slice where the bone tunnel was closed entirely by surrounding bone. This procedure ensured that the longitudinal tunnel region remained identical throughout the repeated measurements (Figure 2). The first 10 cases were

analyzed by 2 readers, and the measurement reliability of relative bone tunnel volume change was analyzed from baseline to 1 year. The size of the articular bone tunnel aperture was determined by computing the surface area of the first slice of the segmentation.[20]

Clinical Evaluation

Passive knee stability was assessed using the Lachman test (grade 0, 1, or 2 for anteroposterior displacement <3, 3-5, and >5 mm, respectively), pivot shift (grade 0, normal; 1, glide; 2, clunk; 3, gross clunk with locking), and KT-1000 arthrometer.[10] Arthrometer-assessed stability was analyzed as the side-to-side difference in anterior laxity at 67 and 89 N. Patient-reported outcomes of the treatment were assessed with the Tegner Activity Scale (0 = disability because of knee problems, 10 = professional soccer player), Lysholm Knee Scoring Scale (0 = severe symptoms, 100 = no symptoms), and International Knee Documentation Committee subjective knee evaluation form (0 = severe functional deficits, 100 = no functional deficits).

Statistical Analysis

Interreader reliability of bone tunnel volume measurements was assessed by calculating the intraclass correlation coefficient ($ICC_{2,1}$) and associated 95% CI based on a 2-way random-effects model assessing the absolute agreement of a single-measure approach.[31] ICC values were classified as poor (≤0.2), fair (0.21-0.4), moderate (0.41-0.6), good (0.61-0.8), or very good (>0.8).[2]

The primary outcome of relative bone tunnel volume change at both follow-up assessments was first inspected for the presence of confounders related to patient demographics and surgical parameters. Between-group effects were then analyzed through linear regression models, including significant confounders or applying independent-samples *t* tests as applicable. Unless otherwise specified, other parameters were compared between the treatment groups with the independent-samples *t* test or Fisher exact test as applicable.

Lachman and pivot-shift grades were compared between the treatment groups by summing all grade frequencies per group over all follow-up periods and applying a Fisher exact test. KT1000 arthrometer side-to-side differences over the entire follow-up period were compared between the groups using mixed-effects linear models with a diagonal covariance structure and restricted maximum likelihood estimation including the baseline value as a covariate. In case these models indicated significant between-group effects, pairwise post hoc independent-samples *t* tests with Bonferroni correction were applied, assessing each follow-up period separately. Postoperative patient-reported outcome scores were analyzed analogously to KT1000 arthrometer measurements. The analysis was conducted in R (R Core Team) and SPSS Statistics for Windows (Version 27.0; IBM). $P < .05$ was considered statistically significant.

RESULTS

Patient Characteristics

The study design and study recruitment flow are summarized in Figure 3. Patient demographics and history are summarized in Table 1. The distribution of surgical parameters between the treatment groups is summarized in Table 2.

Adverse Events

There were 8 and 10 adverse events in the intervention and control groups, respectively ($P = .768$) (Appendix Table A1). In both groups, 2 patients experienced a partial ACL rerupture.

Technical Feasibility

Operating time did not differ between groups (56 ± 10 vs 57 ± 8 minutes; $P = .681$). In 1 case, the OCS was not completely inserted into the bone tunnel as revealed by the baseline CT. Its position, however, remained unchanged in both follow-up CT scans, and no additional action was taken.

Bone Tunnel Enlargement

The procedure applied to assess relative bone tunnel volume change yielded very good interreader reliability (ICC, 0.808; 95% CI, 0.281-0.952). Femoral bone tunnel volume at baseline was larger in the intervention group as compared with the control group (1362 ± 204 vs 1259 ± 173 mm^3; $P = .047$). In femoral aperture cross-sectional area, this difference was nonsignificant (62.8 ± 8.5 vs 58.0 ± 14.9 mm^2; $P = .148$). Similarly, there was a tendency in the intervention group for larger tibial bone tunnel volume (2915 ± 512 vs 2692 ± 618 mm^3; $P = .147$) and bone tunnel aperture cross-sectional area at baseline (69.3 ± 8.8 vs 63.0 ± 15.6 mm^2; $P = .097$). No statistically significant confounding by patient demographics was identified on relative femoral bone tunnel volume change. Over the course of 1 year, relative femoral bone tunnel volume change did not differ between the intervention and control groups (4.5 months, 36% ± 25% vs 40% ± 25% [$P = .644$]; 1 year, 19% ± 20% vs 17% ± 25% [$P = .698$]). Relative tibial bone tunnel volume change, however, was significantly smaller in the intervention group at the 4.5-month follow-up. No statistically significant differences in relative tunnel aperture cross-sectional area were found (Figure 4).

Knee Stability

There were no significant differences in any knee stability outcome (Table 3).

Patient-Reported Outcomes

Patient-reported outcomes did not differ significantly between the treatment groups (estimated effect sizes for

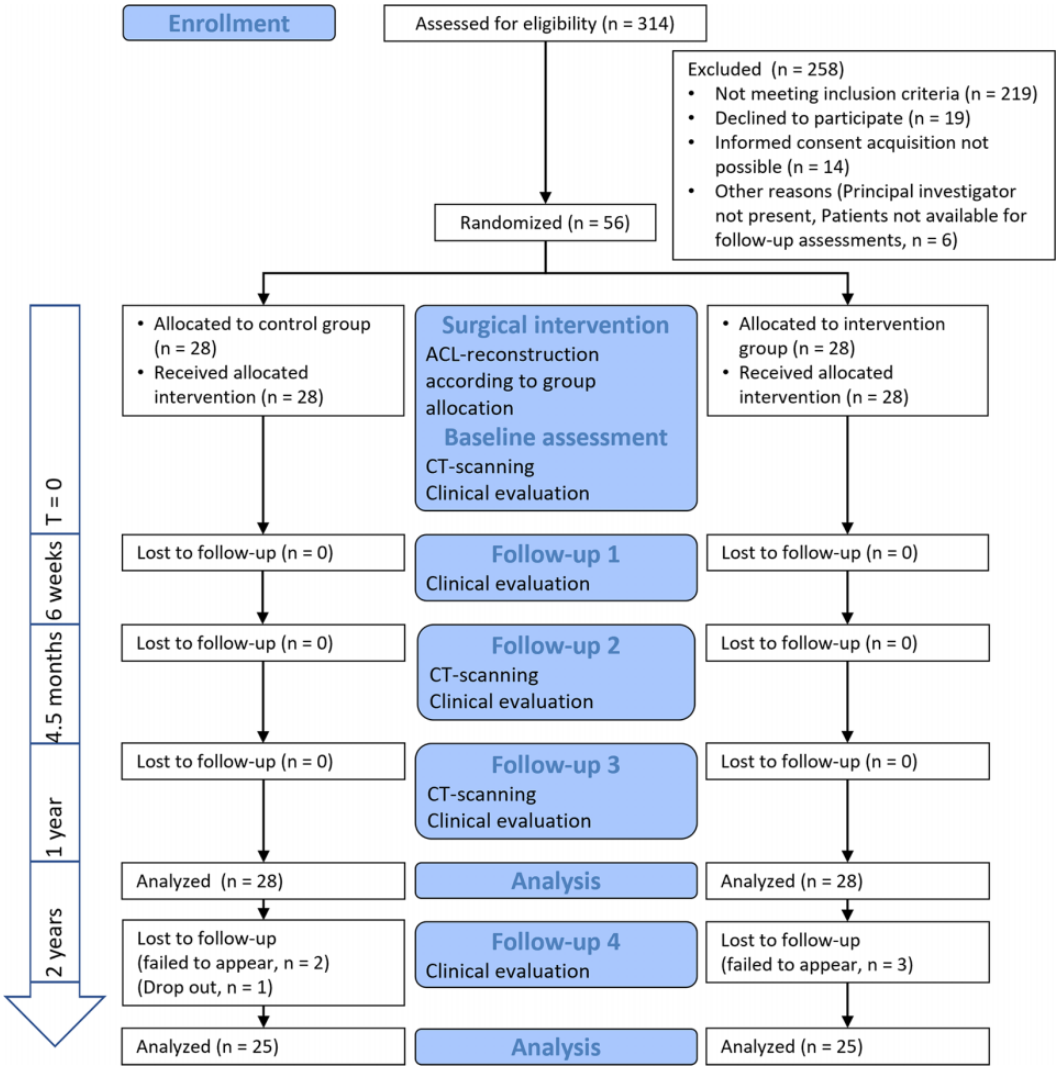

Figure 3. CONSORT (Consolidated Standards of Reporting Trials) flow diagram. The primary end point was relative change in femoral bone tunnel volume 1 year after the surgical intervention. ACL, anterior cruciate ligament; CT, computed tomography.

TABLE 1
Demographics and Patient History[a]

	Control Group (n = 28)	Intervention Group (n = 28)	*P*
Age, y	29.8 ± 8.0	26.6 ± 6.5	.056
Body mass index	25.1 ± 3.1	23.7 ± 3.2	.053
Male	16	19	.582
Smoker	1	10	**.005**
Time to surgery, d	103.1 ± 91.9	116.1 ± 125.6	.333
Type of activity during injury			.352
Sports	27	24	
Activities of daily living	1	3	
Work	0	1	

[a]Data are reported as mean ± SD or absolute values. Bold *P* value indicates statistically significant difference between groups ($P < .05$).

the intervention group): Tegner Activity Scale (0.31; 95% CI, 0.02 to 0.65 [$P = .064$]), Lysholm knee score (–0.30; 95% CI, –2.85 to 2.25 [$P = .816$]), and International Knee Documentation Committee subjective knee evaluation form (0.87; 95% CI, –1.70 to 3.44 [$P = .507$]) (Figure 5).

TABLE 2
Surgical Parameters[a]

	Control Group	Intervention Group	*P*
Additional surgical procedures			.683
Partial meniscectomy	6	5	
Meniscal repair	8	4	
Plica resection	7	7	
Autograft composition			.457
Semitendinosus (4×)	21	18	
Semitendinosus (4×) with gracilis (2×)	6	10	
Semitendinosus (4×) with gracilis (4×)	1	0	
Femoral tunnel			
Diameter bone tunnel, mm	8.66 ± 0.62	9.34 ± 0.51	**<.001**
Diameter tendon graft, mm	8.61 ± 0.57	9.27 ± 0.50	**<.001**
Use of dilator	17	26	**.010**
Tibial tunnel			
Diameter bone tunnel	8.82 ± 0.61	9.34 ± 0.47	**<.001**
Diameter tendon graft	8.68 ± 0.60	8.91 ± 0.55	.134
Use of dilator	18	24	.121

[a]Data are reported as mean ± SD or absolute values. Bold *P* values indicate statistically significant difference between groups ($P < .05$).

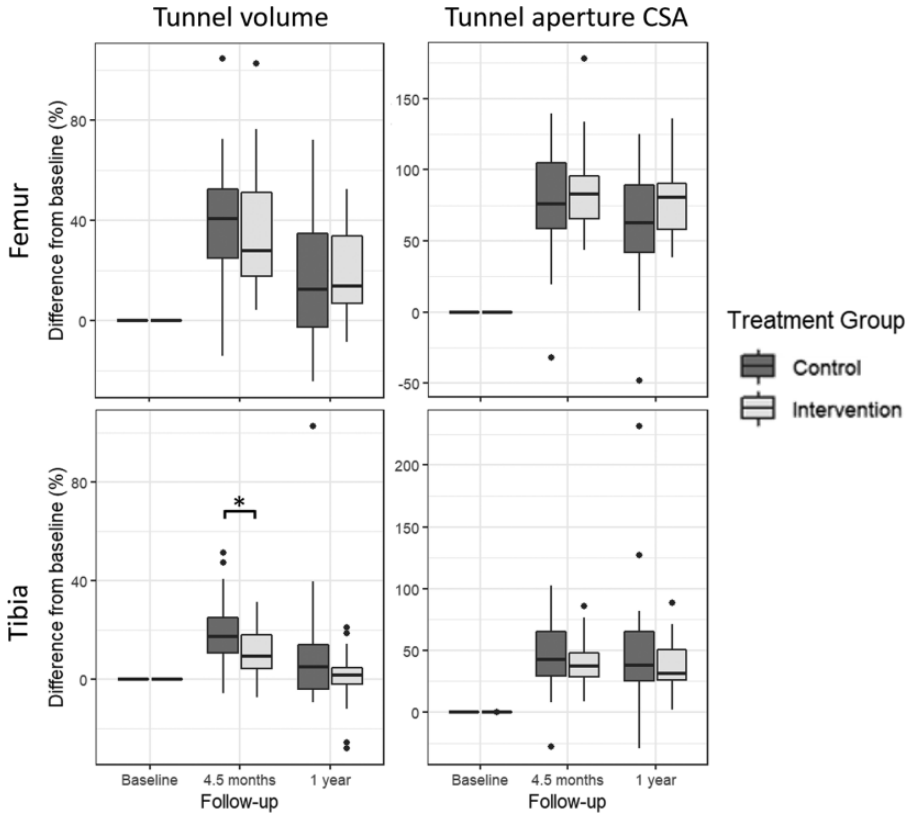

Figure 4. Bone tunnel enlargement expressed as relative bone tunnel volume change and aperture cross-sectional area (CSA) change between the treatment groups. Values are presented as median (horizontal line), interquartile range (box), range (error bars), and outliers (circles). *$P < .05$.

DISCUSSION

This study assessed secondary femoral press-fit fixation of a hamstring tendon autograft with an OCS as compared with graft-only press-fit fixation. Specifically, we assessed the procedure in terms of safety, technical feasibility, and efficacy as defined by functional outcome and BTE. The interventional approach appears to be safe with regard to

TABLE 3
Knee Stability[a]

	Control Group (n = 28)					Intervention Group (n = 28)					
	Baseline	6 wk	4.5 mo	1 y	2 y	Baseline	6 wk	4.5 mo	1 y	2 y	*P*
Lachman grade											.748
0	2	28	27	26	24		28	25	26	24	
1	9		1	2	1	8		3	2	1	
2	17					20					
Pivot-shift grade											.171
0	7	28	27	28	24	6	28	26	25	23	
1	15		1		1	12		2	3	2	
2	5					9					
3	1										
Anterior laxity SSD, mm											
67 N	0.75 ± 0.95	0.46 ± 1.05	0.26 ± 0.71	0.45 ± 0.95	0.25 ± 0.50	0.73 ± 0.83	0.48 ± 0.92	0.43 ± 0.67	0.16 ± 0.47	0.10 ± 0.32	.589
89 N	1.20 ± 1.55	0.93 ± 1.47	0.49 ± 1.23	0.75 ± 1.48	0.51 ± 0.66	1.21 ± 1.12	0.75 ± 1.07	0.75 ± 1.12	0.61 ± 0.93	0.36 ± 0.70	.741

[a]Data are reported as mean ± SD or absolute values. Blank cells indicate values of zero. SSD, side-to-side difference.

repair failure, with an equal number of reruptures in both groups and a rerupture rate (7.1%; 95% CI, 0.8%-23.5%) in line with previous results (4.8%; 95% CI, 3.2%-6.4%).[6] Enlacing an OCS into the hamstring tendon graft was feasible, with only 1 technical complication, where the OCS was not completely inserted into the bone tunnel without adversely affecting the patient's recovery process. The additional work step during graft preparation did not add burden to the standard clinical workflow.

Regardless of treatment group, on average, we observed an increase in bone tunnel volume in the femoral as well as tibial tunnel in the first 4.5 months, with a small decrease at 1 year. The observation of BTE in the early stage, followed by limited closure of the tunnel, agrees with reports from the literature[7,35] and underlines the necessity of adequately timed follow-up assessments when studying the phenomenon.

The intervention under review did not reduce femoral BTE as quantified by the total tunnel volume and tunnel aperture cross-sectional area. In a smaller study cohort with shorter follow-up, Hollis et al[16] assessed the effect of secondary tendon graft fixation with an autogenous bone plug inserted into the femoral tunnel next to the tendon graft. Similarly, they did not find a reduction in BTE. Technically, our approach differs from theirs insofar as the OCS is enwrapped into the tendon graft during graft preparation. The procedure for surgical insertion of the graft is hence unaltered, and the surface area between tendon graft and the osteoconductive material is maximized. However, 3 investigations reported a beneficial effect of bone plug secondary fixation on BTE when used in the tibial tunnel.[1,18,22] This apparent discrepancy may be a result of different primary etiologic factors at play. Whereas the tendon graft is bent at the femoral aperture by approximately 70°,[15,21,33] in the tibia the graft exits the tunnel almost straight, irrespective of the knee flexion angle. Consequently, graft tension yields higher graft-bone contact pressure in the femoral tunnel, which may induce cell necrosis and subsequent bone resorption.[36] Indeed, higher graft bending was associated with increased femoral BTE in previous studies.[24,30,33]

The addition of an OCS in femoral graft fixation significantly reduced relative tibial bone tunnel volume change at 4.5 months. One possible confounder related to this finding is the fact that the addition of the OCS increases the graft diameter. Since the graft was deployed transtibially, the tibial tunnels were drilled to accommodate the larger graft, regardless of the graft diameter on the tibial side. Consequently, tibial tunnels in the intervention group had a larger graft tunnel offset on average, which may have biased the observed group effect.

As is evident by the increased bone tunnel volume at baseline and larger mean drill diameter, enlacing an OCS into the tendon graft effectively increased graft diameter. Despite the lack of efficacy on BTE, the approach may therefore be of use in revision ACL reconstructions where the available graft material has a lower diameter than required relative to the existing bone tunnels. In such cases, the OCS may serve as a space filler with minimal additional burden to the workflow.

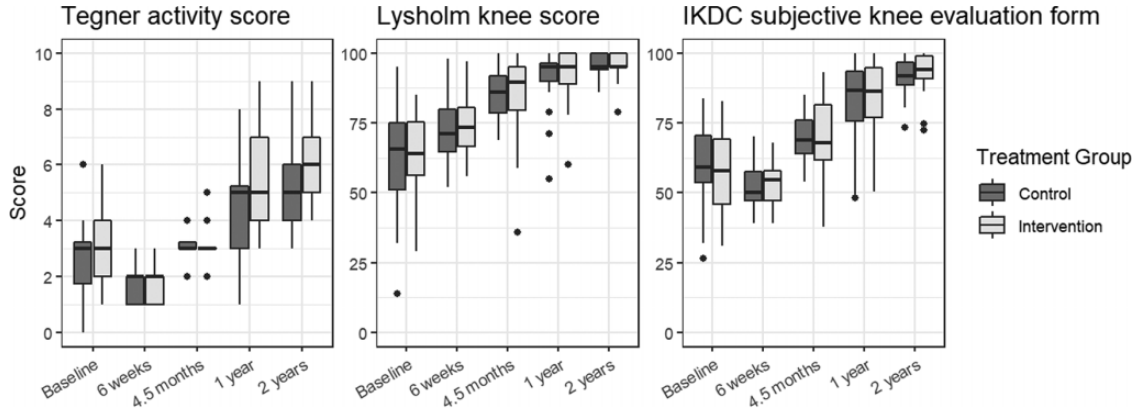

Figure 5. Patient-reported outcome scores between the treatment groups over the course of the trial. Values are presented as median (line), interquartile range (box), range (error bars), and outliers (circles). IKDC, International Knee Documentation Committee.

Limitations

Patient randomization resulted in unbalanced groups with regard to smokers (10/28 intervention group vs 1/28 control group) and the frequency of meniscal repairs (4/28 intervention group vs 8/28 control group). Tobacco consumption impairs tissue healing and revascularization[14] and has been associated with inferior functional outcome after ACL reconstruction.[19,27] Patients receiving meniscal repair were administered a different rehabilitation protocol with prolonged knee unloading, which has been associated with decreased BTE.[5,37] Although our confounder analysis did not indicate it, some degree of confounding of the estimated group effect on BTE might nevertheless have been present.

Of further note, at the present stage, we cannot attribute the lack of efficacy of the interventional approach on BTE to the design and positioning of the OCS, its material composition, or both. The former likely affects the local mechanical regime, and the latter influences the biologically driven response of the tendon graft and the surrounding bone. The use of different materials, such as autogenous bone or other osteogenic compounds, may be investigated in future studies.[13,26]

CONCLUSION

Whereas deploying an OCS at the femoral tunnel aperture as done here is safe and operationally feasible, we did not find substantial evidence of improved graft-to-tunnel incorporation.

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APPENDIX

TABLE A1
Adverse Events[a]

Adverse Event	Time to Event, wk	Clinical Response	Patient Outcome
	Intervention group (n = 7)		
Pretibial hematoma with persistent secretion	2	Surgery	Recovered
Cyclops syndrome	22	Surgery	Ongoing treatment
Persistent pain	29	Surgery	Unknown; lost to follow-up
Extension deficit	53	Surgery	Recovered
Partial ACL rerupture	79	Nonoperative treatment	Recovered
Cyclops syndrome	109	Surgery	Recovered
ACL rerupture with potential meniscal damage	127	Surgery	Recovered

(continued)

Table A1 (continued)

Adverse Event	Time to Event, wk	Clinical Response	Patient Outcome
Control group (n = 9)			
Cyclops syndrome	17	Surgery	Recovered
Meniscal lesion	22	Surgery	Recovered
Cyclops syndrome	40	Surgery	Recovered
Posterolateral tibia plateau fracture after distorsion trauma	46	Surgery	Recovered
Meniscal lesion	53	Surgery	Recovered
ACL rerupture	57	Surgery	Ongoing treatment
Meniscal lesion, cyclops syndrome	59	Nonoperative treatment	Recovered
ACL rerupture	76	Surgery	Unknown; lost to follow-up
Meniscal lesion	80	Nonoperative treatment	Recovered

[a]ACL, anterior cruciate ligament.