Anterior Cruciate Ligament Reconstruction with Autologous Ruptured Tissue: Pilot Clinical Trial

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Disclosures:

Introduction: Most surgical procedures for anterior cruciate ligament reconstruction (ACLR) involve the healing of tendon grafts in a surgically created bone tunnel; however, the attachment between the tendon and the bone is the weakest part of the reconstruction in the early post-transplantation period. Secure fixation of the tendon graft to the bone is thus a significant factor in allowing earlier and more aggressive rehabilitation and earlier return to sports and work. Current treatment with hamstring grafts achieves satisfactory anteroposterior and rotatory stability but causes significant tunnel enlargement. Tissue engineering using stem cells has recently been explored to achieve early healing and better tendon-bone integration. Blood vessels have a richer supply of stem/progenitor cells with characteristic expression of CD34 surface markers, and Matsumoto T et al. demonstrated the presence in sub-acute ly ruptured ACL tissues of CD34-expressing vascular cells with potential for multi-lineage differentiation that can be recruited to the ACL rupture site to support healing [1]. In addition, Mifune Y et al. demonstrated that human ACL-derived CD34+ cells contributed to tendon-bone healing via angiogenesis/vasculogenesis and osteogenesis in an immunodeficient rat model of ACLR [2]. Based on the abundance of CD34+ cells in ruptured (44.3%) vs. intact (8.3%) ACL tissue [1] and the contributions of non-selected cells as well as CD34+ cells to tendon-bone healing in a rat model of ACLR [2], Matsumoto T et al. confirmed the effectiveness of ruptured tissue for early tendon-bone healing in a preclinical study using a canine ACL reconstruction model [3]. Given this background, we hypothesized that the use of autologous ruptured tissue in ACLR would improve clinical results over conventional ACLR by reducing tunnel enlargement. This study aimed to compare the clinical results of double-bundle (DB) ACLR with and without suturing of the autologous ruptured tissue to the grafts in patients with sub-acute ACL injury.

Methods: This phase I/II clinical trial was a prospective and randomized evaluation of the safety, feasibility, and efficacy of ACLR using autologous ruptured tissue in patients with sub-acute ACL injury. The study protocol conformed to the Declaration of Helsinki and was approved by the ethics committees of our university. All patients provided informed consent to participate. The inclusion criteria were (a) ACL insufficiency, (b) ability to undergo surgery within 3 months after injury, (c) male or female aged 15-40 years (closed epiphysis), and (d) provision of written informed consent. The patients who met these criteria were randomized to undergo 1 of the 2 reconstructive procedures according to the envelope method. Ten patients with ACL rupture were randomly allocated to undergo DB ACLR with suturing of the ruptured tissue to the grafts (Fig. 1) or conventional DB ACLR (n=5 each). The ruptured tissue group comprised 3 women and 2 men with a mean age of 23.6±5.1 (range, 16-30) years and the conventional group 2 women and 3 men with a mean age of 27.4±7.4 (range, 19-39) years. The time from injury to surgery was 7.4±2.6 (range, 6-12) weeks for the tissue group and 10.4±2.6 (range, 6-12) weeks for the conventional group. The primary endpoint of the study was knee stability after 2 years according to the Lachman test, anterior laxity under maximum manual stress using a KT-1000 arthrometer and pivot shift test results. As a secondary endpoint, second-look arthroscopic evaluation was performed 1 year postoperatively to classify each transplanted bundle graft based on its thickness and apparent tension. In addition, tunnel enlargement was assessed 3 weeks and 1 year postoperatively using three-dimensional multi-detector row computed tomography (3D-MDCT).

Results: The mean Lysholm score 2 years after ACLR was 92.6±8.4 (range, 79-100) points in the tissue group and 93.0±6.7 (range, 85-100) points in the conventional group (no significant difference). The anterior stability of the knee as measured using the KT-1000 arthrometer after 2 years was 1.4±0.9 (range, 0-2) in the tissue group and 1.0±1.4 (range, 0-3) in the control group (no significant difference). The manual pivot shift test also showed no significant difference between the groups. The rate of negative manual pivot shift test was 4/5 (80%) in both groups. On the second-look arthroscopy assessment, although the graft thickness and apparent tension did not differ significantly between the groups, the synovial coverage tended to be better in the tissue group. Therefore, the AM bundle graft was rated excellent overall in 5/5 (100%) of the tissue group and 4/5 (80%) of the control group (no significant difference). The PL bundle graft was rated excellent in 4/5 (80%) of the tissue group and 3/5 (60%) of the control group (no significant difference).
Assessment of tunnel volume by 3D-MDCT showed less enlargement in the tissue group than in the control group for both the AM and PL at both the femoral (Fig. 2) and tibial sites. The ratios of tunnel volume enlargement in the femur were 84.6±15.9% for the AM and 84.2±14.0% for the PL in the tissue group versus 119.5±24.1% for the AM and 151.3±23.8% for the PL in the control group, differing significantly (p<0.05) for both the AM and PL. The ratios of tunnel volume enlargement in the tibia were 71.0±11.2% for the AM and 65.8±10.8% for the PL in the tissue group versus 77.8±15.4% for the AM and 96.9±30.5% for the PL in the control group (no statistically significant difference for either AM or PL).

Discussion: The Lysholm score, anterior laxity measured using a KT-1000 arthrometer, rotator instability according to the pivot shift test, and second-look arthroscopic evaluation results did not differ significantly between ACLR using ruptured tissue and the conventional technique. However, ACLR using ruptured tissue produced less tunnel enlargement as assessed by MDCT, warranting further long-term follow-up to elucidate its effectiveness.

Significance: ACL ruptured remnant tissue have an advantage in reducing tunnel enlargement in ACLR. ACL ruptured tissue containing abundant vascular stem cells can be clinically used and useful for primary ACL reconstruction at the acute phase.

Acknowledgments: