Revascularization of a Human Anterior Cruciate Ligament Graft During the First Two Years of Implantation


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ABSTRACT

The blood supplies of 45 unimpinged, human anterior cruciate ligament grafts were studied during the first 2 years of implantation. Grafts were defined as unimpinged by the low signal intensity of the graft observed on a sagittal proton density magnetic resonance scan. Magnetic resonance imaging with the intravenous contrast agent gadolinium diethylenetriamine pentacetic acid was used to evaluate the blood supply of the hamstring autograft as well as the periligamentous tissues by assessment of enhancement patterns after administration of the agent. The unimpinged anterior cruciate ligament graft acquired no discernible blood supply during the 2 years of implantation. The graft retained the same hypovascular appearance as the normal posterior cruciate ligament. In contrast, the periligamentous soft tissues were richly vascularized and covered the graft by 1 month. The viability of an unimpinged, human anterior cruciate ligament graft may depend more on synovial diffusion than on revascularization.

It has been suggested that the long-term survival of an ACL graft may depend on its revascularization.¹,³,⁶,⁷ Therefore, studies designed to increase our knowledge of the blood supply of ACL grafts may improve our reconstruction techniques.¹⁰

Controversy exists concerning the process of revascularization of human ACL grafts. Johnson²⁰ believed that previous reports¹,‡,° have led to erroneous conclusions regarding the vascular appearance of the grafts because of an inaccurate biopsy site of the reorganizing fibrous tissue surrounding the tendon graft instead of the tendon material itself. Johnson studied the histologic appearance of ACL grafts and concluded that the graft was a composite consisting of the original hypovascular tendon graft and a surrounding hypervascular reactive fibrous tissue.

Other studies using second-look arthroscopies have evaluated the blood supply of the periligamentous tissues that cover the anterior surface of the graft,²⁷,²⁸,³⁰,³¹ but an understanding of the blood supply of the graft itself has remained elusive because it is hidden inside this vascular, synovial covering.²⁷

Magnetic resonance imaging can distinguish an ACL graft from periligamentous soft tissue.¹³⁻¹⁵,¹⁷ Magnetic resonance imaging combined with the intravenous contrast medium gadolinium diethylenetriamine pentacetic acid (Gd-DPTA) has been shown to be comparable to histology in grading the vascularity of pannus in the rheumatoid knee.²²

This study was designed to characterize the blood supply of a human ACL graft during the first 2 years of implantation by assessing the degree of enhancement after administration of Gd-DPTA with T₁-weighted magnetic resonance imaging.

MATERIALS AND METHODS

Patient selection

From a consecutive series of 67 ACL reconstructions, 48 patients fulfilled the following selection criteria and were admitted into the study: 1) the patient agreed to receive an intravenous injection of the contrast medium Gd-DPTA (Magnevist, Schering, Germany), 2) the authors anticipated that the patient would return for a 1-year follow-up examina-
tion, and 3) the reconstruction was performed using a technique that prevented roof impingement of the graft. Three of the 48 patients (6%) included in the study were later found to have impinged grafts on magnetic resonance scanning. These knees were excluded from the statistical analysis of the enhancement pattern of the 45 knees without roof impingement; however, a description of the enhancement pattern of the impinged grafts is included in the “Discussion” for completeness. Conclusions regarding the clinical success of the reconstruction should not be drawn from this study because of the bias in the selection process.

Brief overview of surgical technique

Each knee had a double-looped, gracilis and semitendinosus ACL autograft inserted arthroscopically without roof impingement. Roof impingement is avoided when the anterior surface of the graft does not contact the intercondylar roof with the knee in maximum extension. The tibial guide pin was drilled to lie 4 to 5 mm posterior and parallel to the slope of the intercondylar roof in the maximally extended knee. After reaming the tibial tunnel, the outlet of the intercondylar notch was enlarged by resecting bone from the intercondylar roof as well as from the medial edge of the lateral femoral condyle until a metal rod the same diameter as the tibial tunnel could be advanced through the tibial tunnel and into the notch with the knee in maximum hyperextension.

Magnetic resonance scanning technique

Imaging was performed with a 1.5-T superconducting magnet (Philips, Medical System International, Da Best, Netherlands) and a dedicated wraparound knee coil. An intravenous infusion line was established in the patient before centering the knee in the bore of the magnet. A T1-weighted (repetition time [TR] of 325, and echo delay time [TE] of 20), oblique coronal localizer was obtained to identify the longitudinal axis of the ACL graft using a 4-mm slice, two signal acquisitions, field of view of 200 mm, and a 140 X 256 matrix. Next, an intermediate weighted (TR = 1200, TE = 40) spin echo sequence was performed using an oblique sagittal imaging plane centered on the long axis of the graft to assess the graft for signs of roof impingement (see Figs. 1A and 2A). The intermediate weighted sequence used a 3-mm slice with a 0.3-mm interslice gap, one signal acquisition, a field of view of 300 mm, and a 512 X 512 matrix.

Forty-five knees had unimpinged grafts and three knees had impinged grafts. Two baseline preinfusion, T1-weighted (TR = 618, TE = 22), spin echo sequences were performed. First, the oblique sagittal view of the graft was repeated using a T1-weighted imaging sequence (TR = 618, TE = 22) in place of the pro-ton density scanning parameters (TR = 1200, TE = 40) (see Figs. 1B and 2B). Second, an oblique axial view of the graft was obtained using 11, 3-mm slices, 4 signal acquisitions, a field of view of 200 mm, and a 192 X 256 matrix in an oblique axial scanning plane transverse to the long axis of the ACL graft (see Figs. 1D, 2C, and 3, B and D). The orientation of the oblique axial view was aligned perpendicular to the longitudinal axis of the graft, which was determined from the oblique sagittal view (Figs. 1C and 3A). The entire intraarticular pathway and a portion of the graft within the tibial tunnel was obtained using the 36 mm of available coverage.

The contrast agent Gd-DPTA was infused without moving the patient (0.1 mmol/kg body weight). The T1-weighted scanning sequences were repeated (see Figs. 1, C and E; 2D; and 3, A, C, and E).

Seven studies were performed at 1 month (33 ± 5 days), 14 studies at 3 months (99 ± 16 days), 11 studies at 6 months (186 ± 18 days), 5 studies at 9 months (269 ± 10 days), 9 studies at 12 months (360 ± 20 days), and 7 studies beyond 1 year (576 ± 270 days). Five patients agreed to have their knees imaged twice.

Twenty-one knees had both the sagittal and oblique axial pre- and postinfusion scans, with imaging being completed within 14 minutes after the infusion. Twenty-four knees had only the sagittal pre- and postinfusion scans, with imaging being completed within 9 minutes after the infusion. Determination of the individual blood supplies of the periligamentous soft tissues and ACL graft was possible by integrating the information from these pre- and postinfusion scans.

Interpretation of magnetic resonance scans

Two radiologists experienced in musculoskeletal magnetic resonance studies (TEF, KEK) evaluated each scan together. They were unaware of the time interval in which each scan was obtained. Only the sagittal images were graded and the final grade was determined by consensus using the following method. The sagittal pre- and postinfusion scans (TR = 618, TE = 22) were compared for the location and intensity of any enhancement. Tissues that demonstrated no increase in signal on the post-Gd-DPTA images were assigned a grade 1. Minimal-to-moderate enhancement was considered a grade 2. Marked enhancement, equal to the signal intensity of subcutaneous fat, was given a grade 3. Four tissues were analyzed for vascular enhancement: 1) the intraarticular portion of the ACL graft, 2) the periligamentous soft tissues about the ACL graft, 3) the normal posterior cruciate ligament, and 4) the periligamentous soft tissues about the normal posterior cruciate ligament.

The oblique axial images of the graft were carefully inspected for the location of any enhancement within the graft. The oblique axial views were not graded because a statistical analysis could not be performed on the three or four studies that were available at each time interval.

Clinical assessment

A clinical evaluation of the function and stability of the knees was performed at an average of 21 ± 7 months postoperatively with a minimum followup of 1 year. Passive knee extension was measured using a goniometer. Stability was determined using the KT-1000 arthrometer (MED-metric, San Diego, CA) and the pivot shift test. Anterior displacements
Figure 1. A, a proton density (TR = 1200, TE = 40) oblique sagittal image in the plane of the ACL graft showing low, homogeneous signal intensity of the intraarticular portion of the graft consistent with an unimpinged ACL graft. Soft tissue is present between the anterior surface of the ACL graft and the intercondylar roof (arrowhead). The tibial tunnel is posterior and parallel to the slope of the intercondylar roof (dotted line). The graft does not angle around the distal edge of the intercondylar roof. B, precontrast T1-weighted (TR = 618, TE = 22) oblique sagittal image shows the periligamentous soft tissues that surround both the ACL graft and normal posterior cruciate ligament have a low signal intensity before administration of Gd-DTPA. C, T1-weighted (TR = 618, TE = 22) oblique sagittal image shows the periligamentous soft tissues about the ACL graft and the
were recorded to the nearest 0.5 mm during a manual maximum translation. Stability was expressed as the difference in translation between the reconstructed and normal knees.4,8 The lateral pivot shift test was graded. Patient satisfaction and function were determined by assessing the patient’s response to the Lysholm scoring scale and the one-legged hop test.23,26 The one-legged hop for distance is designed to test both strength and confidence in the reconstructed leg. The hop index is defined as the percentage of distance jumped on the reconstructed knee divided by the distance jumped on the normal knee.26

Data analysis

Nonparametric statistics were used to analyze the pattern of enhancement. Differences between the enhancement of the ACL graft, the periligamentous soft tissues that surround the ACL graft, the normal posterior cruciate ligament, and the periligamentous soft tissues that surround the normal posterior cruciate ligament within a time interval were determined using the Kruskal-Wallis test. The tissue(s) with a significant increase in enhancement within each time interval was determined with the Wilcoxon signed rank test. Any time-related change in the enhancement of the ACL graft, the periligamentous tissue about the ACL graft, the normal posterior cruciate ligament, and the periligamentous soft tissue about the posterior cruciate ligament between time intervals was determined using the Kruskal-Wallis test. Descriptive statistics were used to summarize the clinical function and stability of the patient’s knees. Significance was accepted when P < 0.05.

RESULTS

Subjective analysis of unimpinged ACL grafts

Forty-five patients had an unimpinged ACL graft defined by a low, homogeneous magnetic resonance signal intensity throughout the entire intraarticular portion of the graft on the proton density scan (TR = 1200, TE = 40) (Fig. 1A). A space was always present between the anterior surface of the ACL graft and the intercondylar roof. The tibial tunnel was aligned entirely posterior and parallel to the slope of the intercondylar roof. There was no angulation of the graft around the intercondylar roof to suggest impingement by the roof.11,13,15,17

Comparing the pre- and post-Gd-DPTA infusion sagittal views revealed longitudinal enhancement streaks within the ACL graft in four studies. Analysis of the pre- and postinfusion sagittal views alone suggested that these streaks could represent new vessels (Fig. 1B and C). The oblique axial views of the graft in two of the four knees clearly demonstrated that these longitudinal enhancement streaks were caused by invagination of vascularized periligamentous soft tissues between the individual bundles of the composite hamstring graft, and that the graft itself did not acquire any significant enhancement at any of the time intervals (Fig. 1, D and E).

The oblique axial views were helpful in demonstrating how little space the unimpinged ACL graft had within the bony boundaries of the intercondylar notch (Fig. 1, D and E). Each unimpinged graft had only 2 to 3 mm of clearance between the ACL graft and the intercondylar roof.

Statistical analysis of the magnetic resonance appearance of unimpinged grafts

The periligamentous tissue that surrounded the ACL graft enhanced significantly more than the ACL graft at each of the six time intervals. The periligamentous tissue that surrounded the posterior cruciate ligament also enhanced significantly more than the normal posterior cruciate ligament at each time interval. The level of enhancement was similar for the periligamentous tissues that surrounded the ACL graft and the normal posterior cruciate ligament at each time interval. There was no significant difference in the enhancement pattern between the unimpinged ACL graft and the normal posterior cruciate ligament at any time interval, suggesting they may have similar blood supplies (Table 1).

The enhancement of the unimpinged ACL graft (P = 0.49), the periligamentous tissues surrounding the ACL graft (P = 0.99), the normal posterior cruciate ligament (P = 0.23), and the periligamentous tissues surrounding the normal posterior cruciate ligament (P = 0.26) did not change between time intervals during the first 24 months of graft implantation. The enhancement of the soft tissues surrounding the unimpinged ACL graft was as well developed at 1 month as it was between 12 and 24 months.

Clinical analysis of knee stability and function

A clinical assessment of knee stability and function was obtained in 42 of 45 patients. The other three patients moved out of state and were unable to return for followup. The average age of these 8 female and 34 male patients was 26 ± 6 years. Thirty-eight (90%) of the knees had less than 3 mm periligamentous soft tissues about the normal posterior cruciate ligament enhance with intensity equal to that of subcutaneous fat (grade 3) after administration of Gd-DTPA (GAD). Thin, longitudinal enhancement streaks within the ACL graft suggest that there may be new vascularity within the graft. The dotted line marks the location where the oblique axial scans (see Fig. 1D and E) were taken. D, there is a minimal amount of clearance between the intercondylar roof and the anterior surface of the ACL graft on the pre-Gd-DPTA oblique axial view (small arrowhead) (TR = 618, TE = 22). Periligamentous soft tissues infiltrate between the three distinct bundles of the unimpinged ACL graft (two larger arrowheads). E, the periligamentous soft tissues markedly enhance on the post-Gd-DPTA oblique axial view and surround the ACL graft (three arrowheads) (TR = 618, TE = 22). The longitudinal enhancement streaks on the sagittal views are caused by the infiltrating synovium between the graft bundles and not by intrinsic revascularization of the graft itself. L marks the lateral femoral condyle.
Figure 2. A, a proton density (TR = 1200, TE = 40) oblique sagittal image in the plane of the ACL graft showing regionalized increased signal intensity of the intraarticular portion of the graft characteristic of an impinged ACL graft. The intra-articular opening of the tibial tunnel is partially anterior to the slope of the intercondylar roof (dotted line). The intercondylar roof directly contacts the anterior surface of the graft, causing the graft to bow posteriorly (arrowhead). B, a precontrast T1-weighted (TR = 618, TE = 22) oblique sagittal image shows the periligamentous soft tissues are indistinct from the impinged ACL graft. The impinged region of the ACL graft has an increased signal compared with the low signal intensity of the posterior cruciate ligament. C, this impinged ACL graft cannot be distinguished from the surrounding periligamentous soft tissue on the pre-Gd-DPTA oblique axial view (TR = 618, TE = 22). Any remaining graft material is located in the superolateral quadrant of the notch (between dotted line and arrowhead). D, moderate enhancement (grade 2) can be seen in the superolateral quadrant of the notch (between dotted line and arrowhead) in this impinged ACL graft on the post-Gd-DPTA GAD) oblique axial view (TR = 618, TE = 22). Either the vascularized synovium replaced the graft or the impinged graft itself has become hypervascularized in contrast to the hypovascular appearance seen in the unimpinged ACL graft (Fig. 1 E). L marks the lateral femoral condyle.
of anterior translation on the operated knee compared with the normal knee determined by the manual maximum translation test (1.0 ± 1.5 mm). The other four were unstable, with three knees having a grade 1 and one knee having a grade 2 pivot shift test. The average difference in passive knee extension between the reconstructed and normal knee was 1.3° ± 2.2°. Patients rated their knees very functional, with a 95.6% ± 5.8% using the Lysholm scoring scale. The ability to do the one-legged hop for distance on the reconstructed knee was restored in the majority of patients with a hop index of 97.5% ± 5.8%.

DISCUSSION

Infusion of Gd-DPTA has been shown to be comparable with histology in differentiating hypervascular and hypovascular, fibrous pannus in the rheumatoid knee. A T1-weighted FLASH (fast low-angle shot) sequence has been used to dynamically study tissue perfusion within the first 2 minutes of intravenous infusion but has a major disadvantage in that only one section of the knee can be imaged. Fortunately, the enhancement observed during a FLASH sequence persists after a subsequent T1-weighted spin echo sequence. In our study the spin echo sequence in multiple imaging planes was used in preference to the FLASH sequence because it permitted a survey of the enhancement pattern of the entire joint. We believe we are justified in inferring that an increase in the enhancement pattern of a tissue indicates an increase in its vascularity.

Our findings are also supported by the histologic analysis of Johnson of 20 free, autogenous semitendinosus grafts that underwent arthroscopic biopsy from 20 days to 44 months after implantation. He observed after tourniquet release that the surrounding periligamentous fibrous tissue bled profusely, in contrast to the tendon graft, which had no vascularity or bleeding. Histologic analysis of the composite graft revealed the tendon portion had only a few vessels located between collagen bundles, which was easily distinguished from the surrounding proliferating fibrous tissue that was hypervascular.

In our study there was no hypervascular phase in the unimpinged human ACL grafts during the first 2 years of implantation (Fig. 1). In fact, the graft remained hypovascular, similar to the normal posterior cruciate ligament. Ninety percent of the knees with these hypovascular ACL grafts remained stable and functional. Our findings agree with animal studies that have shown that revascularization is not required for graft viability and has no relationship to the strength of the graft.

Animal studies have shown that the periligamentous synovium is the most rapid and extensively vascularized tissue after an ACL reconstruction. Similarly, by 1 month the unimpinged human ACL graft was covered by a periligamentous soft tissue envelope rich in vascularity. This synovial-graft interface may facilitate synovial nutrition, which has been proposed as the principle source of nutrients for cellular proliferation within the graft.

Other authors have proposed that a hypervascular phase occurs within the ACL graft itself but our findings are in disagreement with this observation. This difference in opinion may be explained by the different experimental techniques used in these studies. Vascularity studied by the Spalteholz technique relies on relatively wide sagittal sections that include the entire sagittal width of the relatively narrow canine ACL graft. Because this technique provides only a unidimensional view of the graft, the hypervascularized periligamentous soft tissue may have been superimposed on the graft, making it technically difficult to distinguish the vascularity of the tendon from the surrounding soft tissue.

We believe our study may more closely reflect the actual vascularity of the graft because the narrow-slice, multiple-plane imaging technique reduced the confounding artifacts caused by imaging contiguous tissues. In the unimpinged ACL grafts, the use of the pre- and postinfusion oblique axial and sagittal views allowed clear differentiation between enhancement of ACL graft material and periligamentous soft tissue. The streaks of enhancement seen only on the sagittal postinfusion images suggested the development of longitudinal blood vessels. The oblique axial images of the unimpinged grafts confirmed that these streaks were actually hypervascular, periligamentous tissue invaginated between the individual bundles of the ACL graft preventing us from incorrectly concluding that the graft itself had become extensively revascularized.

During the study we imaged three knees in which the ACL graft was impinged by the intercondylar roof (Figs. 2 and 3). We also reimaged eight additional impinged grafts from an earlier study. Compared with the unimpinged grafts, the bundles of the impinged grafts could not be reliably distinguished from the periligamentous soft tissue on the
Figure 3. A, a postcontrast (GAD) T1-weighted (TR = 618, TE = 22) oblique sagittal image of an impinged ACL graft. Line C-D defines the location of the oblique axial image (see Fig. 3, B and C) that demonstrates the enhancement pattern of the impinged portion of the ACL graft. Line A-B defines the location of the oblique axial image (see Fig. 3, D and E) that demonstrates the enhancement pattern of the unimpinged portion of the ACL graft within the tibial tunnel. B, this impinged ACL graft cannot be distinguished from the surrounding periligamentous soft tissue on the pre-Gd-DPTA oblique axial view (TR = 618, TE = 22). Any remaining graft material is located in the superolateral quadrant of the notch. C, the superolateral quadrant of the notch contains three distinct enhancement patterns on the post-Gd-DPTA (GAD) oblique axial view of an impinged ACL graft (TR = 618, TE = 22). A small, central portion of the graft retains a low signal intensity and does not enhance (grade I), a larger rim of tissue around the graft moderately enhances (grade 2), and a thin portion of tissue at the margin of the notch at 12 to 1 o’clock and from 3:30 to 4:30 markedly enhances (grade 3). It is difficult to determine if the vascularized synovium replaced the graft or whether the impinged graft itself has become hypervascularized. D, the four bundles of the unimpinged por-
tion of the ACL graft within the tibial tunnel have been fused into two dumbbell-shaped grafts on the pre-Gd-DPTA oblique axial view (TR = 618, TE 22). The fibrous tissue within the tibial tunnel has a higher signal intensity than the graft. E, moderate enhancement grade 2) can be seen in the fibrous tissue within the tibial tunnel that surrounds the unimpinged portion of the ACL graft on the post-Gd-DPTA (GAD) oblique axial view (TR = 618, TE = 22). The fibrous tissue does not enhance as much as the synovium that surrounds the impinged portion of the graft in the intercondylar notch (see Fig. 3, A and C). L marks the lateral femoral condyle.

pre-Gd-DPTA sequence (Fig. 2, B and C, and 3B). After the Gd-DPTA infusion, the tissue in the superolateral quadrant of the notch, which should have been occupied by graft material, enhanced to varying degrees (Figs. 2D and 3C). Possible explanations for the different enhancement patterns between the impinged and unimpinged grafts include intrinsic revascularization of the impinged graft, replacement of the impinged graft by vascularized periligamentous tissue, or a combination of these two processes. Clinically, an impinged graft does not function as well as an unimpinged graft, which implies that the hypertensive response associated with graft impingement may be a sign of a graft in trouble.

No correlation has been found between the blood supply of an ACL graft and its tensile strength.24 There is no ad-vantage in retaining the blood supply of a graft over an avascular graft in preventing the rapid adverse changes in mechanical properties that develop postoperatively.5 Cellular repopulation, proliferation, and collagen production within an ACL graft occur before revascularization.21

These animal studies have established that the viability and mechanical properties of an ACL graft are not likely to be related to the evolution of its intrinsic blood supply. In summary, ACL grafts do not go through a period of hypervas-

ularization if they are inserted without roof impingement.

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