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Hindlimb Growth After a Transphyseal Reconstruction of the Anterior Cruciate Ligament

A Study in Skeletally Immature Sheep With Wide-Open Physes

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Background: There is a lot of controversy in the recent literature with regard to the optimal treatment of anterior cruciate ligament (ACL) injuries during growth. Iatrogenic growth disturbance due to physeal damage is a potential complication, forcing many orthopaedic surgeons to treat these injuries conservatively.

Hypothesis: It is possible to perform a fully transphyseal ACL reconstruction in an ovine model with wide-open physes without creating growth disturbances.

Study Design: Descriptive laboratory study.

Materials and Methods: Four-month-old skeletally immature sheep underwent a transphyseal ACL reconstruction of the right knee. The surgical technique followed the criteria known to be essential to avoid growth disturbances in humans; the tibial tuberosity was spared to prevent a genu recurvatum, thermal damage to the growth plates was avoided, the physes were perforated with a small-diameter drill in the center of the growth plate, a soft tissue graft was used, graft fixation was achieved far away from the growth plates, the perforated growth plates were filled by the soft tissue graft, and the graft was moderately pretensioned before fixation. The left knee served as a control. A computer-assisted evaluation of long radiographs (frontal and sagittal plane) of the exarticulated hindlimbs was performed to exactly evaluate the limb alignment, joint orientation, and leg length. The animals were sacrificed in groups of 6 after 3, 6, 12, and 24 weeks.

Results: No angular deformities or leg-length discrepancies occurred after this transphyseal ACL reconstruction procedure throughout the remaining growth.

Conclusion: This large-animal study supports the clinical observation that it is possible to perform an ACL reconstruction without creating growth disturbances as long as a number of key principles are followed.

Clinical Relevance: Previous animal studies argued against ACL reconstruction in skeletally immature patients. This large-animal study provides support for early operative treatment of ACL ruptures even in young patients with open physes.

Keywords: anterior cruciate ligament reconstruction; open physes; children; skeletally immature; large-animal study; sheep model; basic research; growth disturbance; EndoButton

Ruptures of the anterior cruciate ligament (ACL) are diagnosed with increasing frequency.[2,3] Recently, there has been an increased interest in early, aggressive operative management of these injuries to restore stability in skeletally immature patients. However, we are still faced with the question of what to do with a young child with an acute ACL tear.[3,14] Discussion is still ongoing as to whether the benefits of early ACL reconstruction to prevent secondary meniscal tears outweigh the risk of possible growth arrest. Due to iatrogenic growth arrest after surgery, limb-length discrepancies and angular deformities in the frontal and sagittal plane have been reported.[14-16]

In contrast to the field of adult ACL reconstruction, where a wide variety of basic research studies involving animal models have been performed, few such models have been developed for skeletally immature individuals (Table 1).

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TABLE 1
Previous Animal Models Investigating Anterior Cruciate Ligament Reconstruction With Open Physes

Authors	Publication Year	Animal Model	No. of Animals	Aim of Study	Results
Guzzanti et al[10]	1994	Rabbits	21	To correlate amount of growth plate damage to growth deformities	3 growth disturbances (2 tibial valgus deformities, 1 tibial shortening)
Stadelmaier et al[25]	1995	Canine	8	Soft tissue graft vs control with empty tunnels	4 dogs with empty tunnels demonstrated forming of bony bridges
Ono et al[19]	1998	New Zealand White rabbits	56	Soft tissue graft vs bone-tendon-bone graft	46 ruptures of the graft; remaining 10 animals demonstrated tibial deformities
Edwards et al[7]	2001	Canine (beagles)	12	To investigate whether pretensioning causes growth disturbances	All animals demonstrated valgus deformities of the distal femur and varus deformities of proximal tibia
Chudik et al[5]	2007	Canine	25	Different femoral fixation techniques	Graft failure in 36%; 28% of the grafts were attenuated, angular, and rotational deformities
Seil et al[22]	2008	Sheep	18	To evaluate the risk of growth disturbances	Significant valgus deformities if tunnels were not filled with a graft

Recently, several authors have suggested the development of basic research models to better understand the biologic response after ACL rupture and reconstruction in young patients.[2,15,22] Small-animal studies investigating ACL reconstructions in animals with open physes have been performed in both canine and rabbit models (Table 1). All these studies demonstrated severe growth disturbances due to damage to the growth plate.[5,7,10,19,25] The surgical method in the present study implements those criteria identified to be essential to prevent growth disturbances after ACL reconstruction during growth. The aim is to analyze the growth of the hindlimb after a fully transphyseal ACL reconstruction in young sheep with wide-open physes, representing the knee of a girl with a skeletal age between 9 and 12 years.[22] Limb alignment, joint orientation, and leg length of the operated hindlimbs are analyzed and compared with the nonoperated hindlimbs throughout the remaining growth period. We hypothesize that it is possible to safely perform a transphyseal ACL reconstruction without creating growth disturbances, even in very young sheep, as long as certain important criteria are applied to the surgical technique.

MATERIALS AND METHODS

Study Design

All procedures were performed with permission of the local governmental animal rights protection authorities (Ref. No. 05/933) and in accordance with the National Institutes of Health guidelines for the use of laboratory animals. Twenty-four skeletally immature female German black-headed sheep, 4 months of age, underwent an ACL reconstruction using a fully transphyseal technique. The amount of longitudinal growth of 4-month-old sheep corresponds to the amount of remaining growth in girls with a skeletal age between 9 and 12 years.[22] Four groups of 6 animals each were created, and animals were sacrificed at 3, 6, 12, and 24 weeks postoperatively. The contralateral knees with intact ACLs served as controls. The rationale for terminating the experiment at 24 weeks was in accordance with previous animal models.[5,7,10,19,25] The growth rate of 4-month-old sheep is known to be sufficient to create early and severe growth disturbances within 24 weeks.[22] Sexual maturity occurs early in sheep. However, it has been shown that the growth plates remain open even after sexual maturity has been reached.[13] This is true also for the previously used canine model, where at 24 weeks open growth plates were still demonstrable.[5] However, the ratio of growth plate closure to life expectancy is less than in humans, meaning that cessation of longitudinal bone growth occurs relatively early in life.[13] The surgical technique followed the criteria known to be essential to avoid growth disturbances in humans—the tibial tuberosity was spared to prevent a genu recurvatum,[14,23] thermal damage to the growth plates was avoided,[24] the physes were perforated with a small-diameter drill in the center of the growth plate,[8,23,24] a soft tissue graft was used,[8,14] graft fixation was achieved far away from the growth plates,[9,14,24] the perforated growth plates were filled by the soft tissue graft,[4,25] and, finally, the graft was moderately pretensioned before fixation.[7,14]

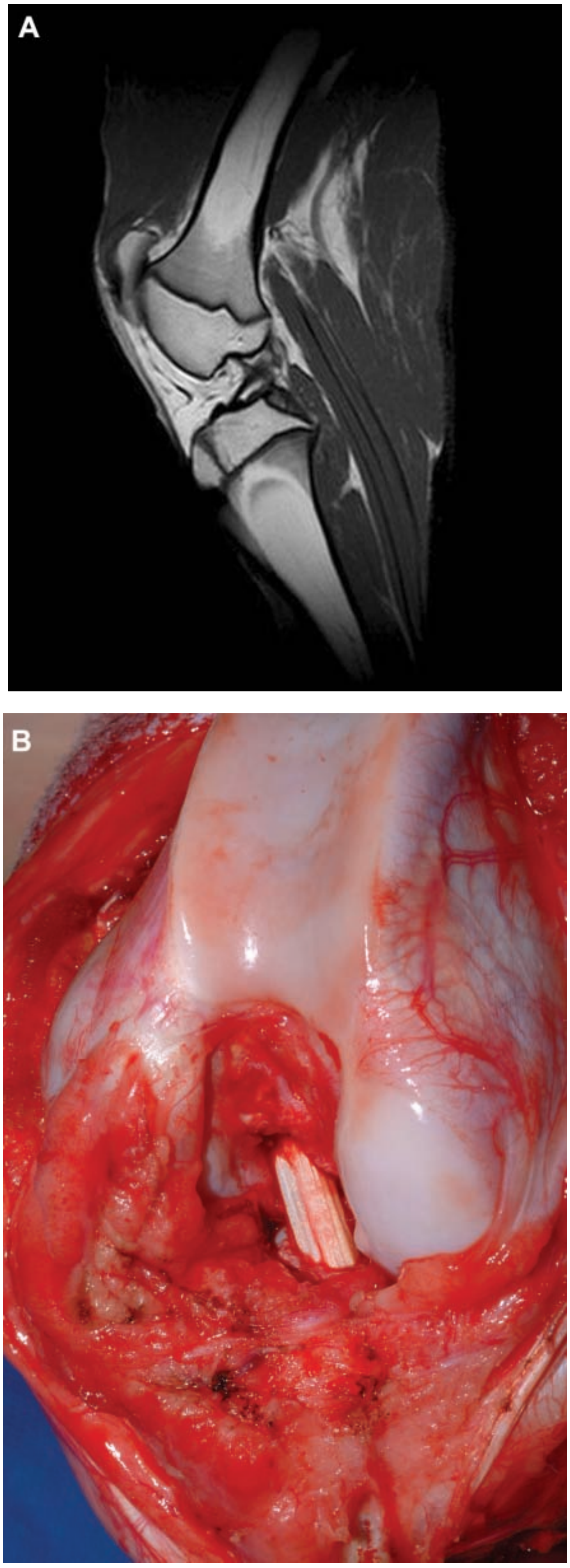

Figure 1. A, MRI scan (T1-weighted image) of a 4-month-old sheep knee, demonstrating wide-open physes. B, intraoperative photograph demonstrating the anteromedial arthrotomy of a right knee with the soft tissue anterior cruciate ligament graft in place.

Operative Procedure

The right knee joint was exposed through an anteromedial incision with release of the medial parapatellar retinaculum. The patella was displaced laterally, the anterior fat pad was sharply separated, and the ACL exposed and removed. The ACL insertion sites were cleared of all remaining soft tissues. A split of the ipsilateral flexor digitorum superficialis tendon was used as an autologous transplant. A longitudinal split of 60-mm length was harvested, aligned to a graft of 4.5-mm diameter, and sewn together at each end with a baseball stitch. A graft diameter of 4.5 mm was chosen because this diameter corresponds to the minimum tunnel width necessary for the use of the EndoButton (Smith & Nephew Endoscopy, Andover, Massachusetts). This diameter accounts for 1.7% of the cross-sectional area of the proximal tibial physis and for 2.8% of the distal femoral physis.[22] A pretension of 5 to 10 lb (2.3 to 4.5 kg) was applied to the graft using the GRAFTMASTER II system and the inbuilt tensiometer (Smith & Nephew Endoscopy, Andover, Massachusetts). A transphyseal tibial tunnel was then created using a hand drill to prevent thermal damage to the growth plate. The apophysis of the tibial tuberosity was safely spared. A transphyseal femoral tunnel was also created using a hand drill. Before fixation, the graft was pretensioned to 20 N after 10 cycles of flexion/extension of the knee joint. Graft fixation was achieved using the EndoButton proximally and the suture washer device (Smith & Nephew Endoscopy, Andover, Massachusetts) distally (Figure 1B).

Measurements

After sacrifice and disarticulation of the hindlimbs from the hip joint, the specimens were frozen at –20°C in full extension with intact soft tissue coverage. Without thawing the specimens, digital long radiographs were obtained in both anteroposterior and lateral views to allow measurements in the frontal and sagittal plane. It was not possible to obtain weightbearing radiographs as the specimens were disarticulated at the hip joint. A spherical body of 30-mm diameter was attached to each limb in the plane of the bony structures to allow later referencing of the radiographs for the computer-aided measurements. All radiographs were taken using a standard protocol. The x-ray tube was positioned 300 cm from the film. The knee joints were fully extended and positioned in a custom-made frame. The x-ray beam was centered at the level of the knee joint with the patella facing directly forward, centered between the femoral condyles. The digital analysis of alignment, joint orientation, and limb length is feasible only when the knees are optimally positioned in a true lateral and anteroposterior view (Figure 2 and Table 2).[21] All radiographs showed the entire lower extremity, including the femoral head, the knee, and the ankle joint.

For computer-aided analysis, the mediCAD planning software was used (Hectec GmbH, Altfraunhofen, Germany; approved by the US Food and Drug Administration).[11] This software features digital analysis of alignment, joint orientation, and leg length. It has been shown that this software improves accuracy and reproducibility compared with

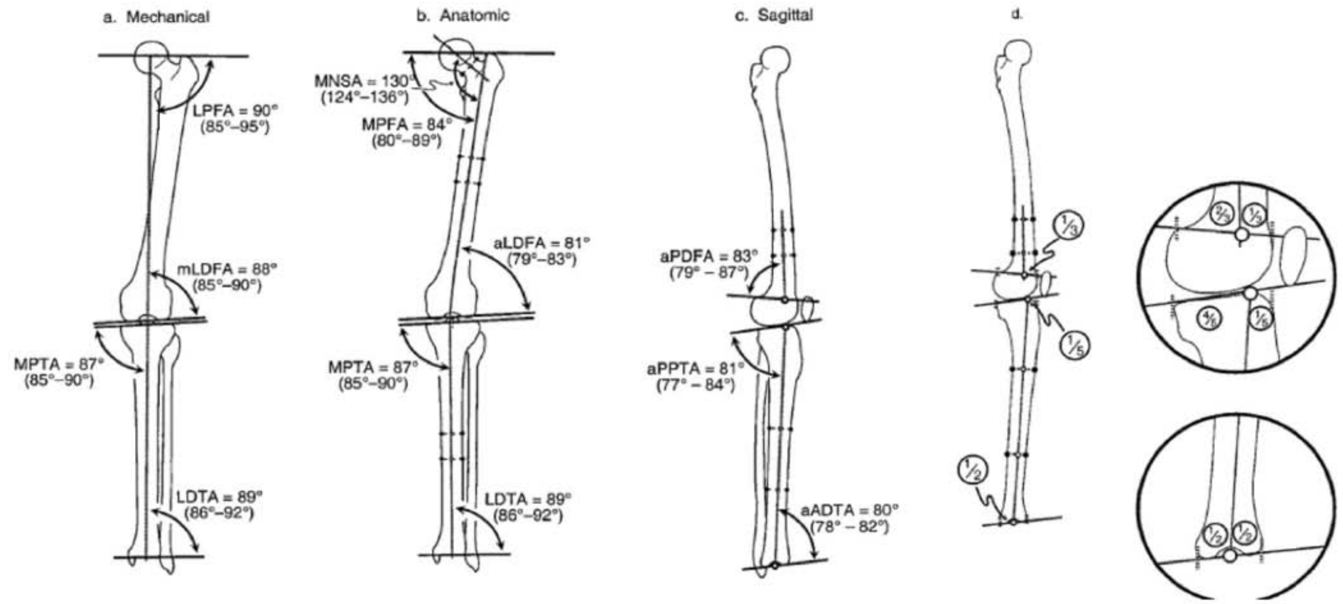

Figure 2. Alignment and joint orientation angles in the frontal (a, b) and sagittal (c, d) plane of the human lower extremity according to Paley.[20,21] (Reprinted with permission from Paley D, Pfeil J. Principles of deformity correction around the knee [in German]. *Orthopade.* 2000;29:18-38.) See Table 2 for nomenclature explanation of most acronyms in this figure. In addition, MNSA, medial neck-shaft angle; MPFA, medial proximal femoral angle; aLDFA, anatomic lateral distal femoral angle; aADTA, anatomic anterior distal tibial angle.

conventional measurements.[11] For determination of the magnification factor of the radiographs, a spherical body of 30-mm diameter was used as a calibration reference. All measurements were done on a "class A" screen approved for diagnostic radiology. The contours of the femur, tibia, and talus were drawn digitally. The mechanical lateral proximal femoral angle, lateral distal femoral angle, medial proximal tibial angle, lateral distal tibial angle, anatomic-mechanical angle, joint-line convergence angle, and mechanical axis deviation were calculated by the software for the frontal plane measurements (Figure 3 and Table 2). The anatomic posterior distal femoral angle and anatomic posterior proximal tibial angle (representing the tibial slope) were calculated for the analysis of the sagittal plane (Figure 4 and Table 2). The abovementioned parameters are those defining the lower leg geometry according to the system of Paley.[20,21] However, this setup did not allow us to determine torsion or rotation of the femur and the tibia. All measurements of the 88 radiographs were repeated 5 times and averaged. The analysis was made by 2 surgeons by consensus review. To eliminate memory effects, the measurements were performed in a random manner on different days.[11] Two of us (S.H. and C.K.) and others have previously shown that the computer-assisted measurement demonstrates a significantly decreased intraobserver variability when compared with conventional measurements.[11]

Statistical Analysis

The data were analyzed using SPSS software (SPSS 11.5, SPSS Inc, Chicago, Illinois). We performed a pre-hoc power analysis where we defined the length and the angulations in the frontal and sagittal plane as a main outcome variable. We set α at .05 and power at 0.85. Power calculations determined that 6 animals were needed per group to detect a 5° difference in varus-valgus angulation and a 5-mm leg-length discrepancy. The average standard deviation of each parameter was calculated and compared between the intact left and operated right knee using a paired *t* test. A *P* value of .05 was considered statistically significant.

RESULTS

Two animals died of pneumonia and had to be excluded from the final evaluation, leaving 22 animals available for the computer-aided measurements (at 3 and 6 weeks 5 animals each; at 12 and 24 weeks, 6 animals each). All grafts were in place, tensioned, and covered by a synovial sheath as early as 3 weeks after surgery.

There was no significant difference in mean longitudinal growth in any of the 22 animals available for computer-aided measurements. There was no limb-length discrepancy when comparing the femoral and tibial lengths of the operated right to the intact left hindlimb. Three weeks after surgery, the mean femoral length of the intact (left) hindlimb was 174.5 ± 11.5 mm; the femoral length of the right hindlimb demonstrated a mean length of 172 ± 11.4 mm ($P > .05$). The mean tibial length of the animals sacrificed at 3 weeks was 185.7 ± 10.1 on the left and 185.1 ± 9.0 on the right side ($P > .05$). The corresponding data (intact left vs operated right) for the animals that survived 6 weeks were 174.7 ± 18.7 mm and 177.8 ± 16.8 mm ($P > .05$) for the femoral and 186.6 ± 15.0 mm and 184.6 ± 17mm ($P > .05$) for the tibial length. The animals that

TABLE 2
Nomenclature of Limb Alignment and Joint Orientation in the Frontal and Sagittal Plane According to Paley[20,21]

mLPFA	Mechanical lateral proximal femoral angle: angle between the mechanical femoral axis and a line from the tip of the greater trochanter to the hip center
mLDFA	Mechanical lateral distal femoral angle: angle between the mechanical femoral axis and a tangent through the 2 most convex distal points of the femoral condyles.
MPTA/mMPTA	Medial proximal tibial angle: angle between the mechanical axis of the tibia and a line along the flat portion of the subchondral bone of the tibial plateau
LDTA/mLDTA	Lateral distal tibial angle: angle between the mechanical tibial axis and a line through the tip of the medial and lateral talus shoulder
AMA	Anatomic-mechanical angle: angle between the anatomical and mechanical femoral axes
JLCA	Joint-line convergence angle: angle between the tangent through the 2 most convex distal points of the femoral condyles and a line along the flat portion of the subchondral bone of the tibial plateau
MAD	Mechanical axis deviation: distance of the mechanical axis of the leg from the knee center
aPDFA	Anatomic posterior distal femoral angle: angle between the anatomic femoral axis and the tangent connecting the anterior and posterior aspect of the femoral condyles in the sagittal plane
aPPTA	Anatomic posterior proximal tibial angle ("tibial slope" angle): angle between the anatomic tibial axis and the tangent connecting the anterior and posterior aspect of the tibial condyles in the saggital plane

were sacrificed after 12 weeks demonstrated a mean femoral length of 181.7 ± 14.1 mm (intact left) and 179.9 ± 12.1 mm (operated right hindlimb) ($P > .05$). The corresponding data for the tibial length 12 weeks after surgery were 194.5 ± 12.4 mm and 196.1 ± 14.4 mm ($P > .05$). Finally, the animals sacrificed 24 weeks after the ACL reconstruction revealed a mean femoral length of 187.7 ± 17.8 mm on the left and 184.4 ± 14.3 mm on the right hindlimb, again without a significant difference ($P > .05$). The tibial measurements in that group demonstrated a mean length of 204.9 ± 13.3 mm of the intact and 206.5 ± 11.7 mm of the operated leg ($P > .05$).

The alignment of the hindlimbs demonstrated no side-to-side differences with a mean mechanical axis deviation of 11 ± 2 mm versus 10 ± 2 mm ($P > .05$) throughout the time of observation. The joint orientation in the frontal and sagittal plane revealed no statistically significant angular deformity between the paired knees. Relative values of the computer-assisted analysis are shown in Figure 5.

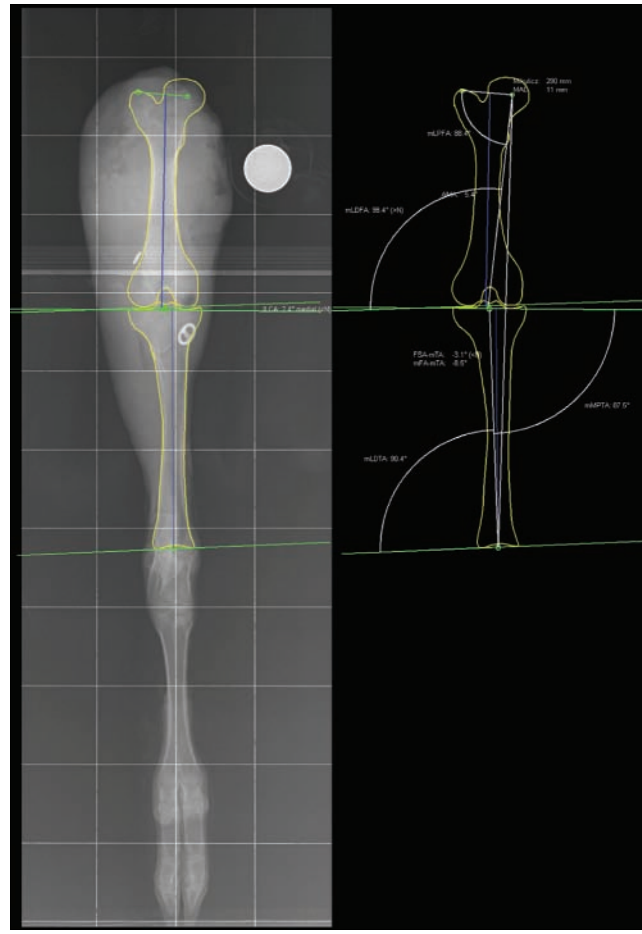

Figure 3. Long anteroposterior radiograph of an operated (right) hindlimb. The spherical body of 30-mm diameter is positioned in the plane of the bones and is used for calibration. The mechanical lateral proximal femoral angle (mLPFA), mechanical lateral distal femoral angle (mLDFA), medial proximal tibial angle (mMPTA), lateral distal tibial angle (mLDTA), anatomic-mechanical angle (AMA), joint-line convergence angle (JLCA), and mechanical axis deviation (MAD) are automatically generated and displayed by the software. FSA-mTA, angle between the femoral shaft axis and the mechanical tibial axis; mFA-mTA, angle between the mechanical femoral axis and the mechanical tibial axis.

DISCUSSION

The goal of this study was to analyze the geometry of the lower limb after a transphyseal ACL reconstruction in skeletally immature sheep with wide-open physes. As the focus was set on growth disturbances, we did not directly study the growth plate of these animals. The computer-aided analysis in the frontal and sagittal plane revealed no statistically significant differences of the alignment, joint orientation, and leg length when comparing the operated right and the intact left hindlimb. Thus the data confirm our hypothesis that it is possible to perform an ACL reconstruction in very young

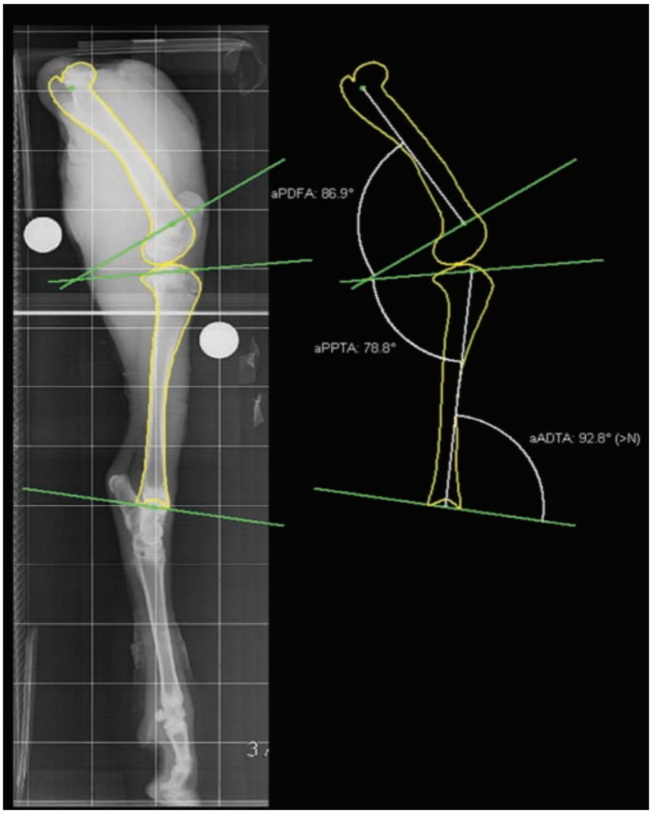

Figure 4. Long lateral radiograph of a nonoperated (left) hindlimb. The spherical bodies of 30-mm diameter are positioned in the plane of the bones and are used for calibration. The anatomic posterior distal femoral angle (aPDFA) and anatomic posterior proximal tibial angle (aPPTA), representing the tibial slope, are automatically calculated and displayed by the software.

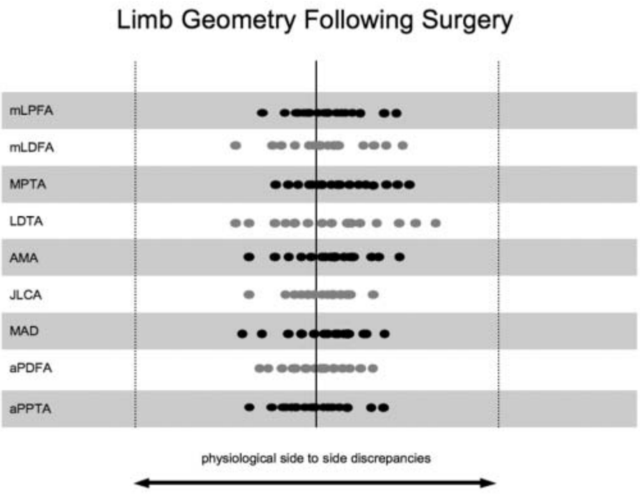

Figure 5. Alignment and joint orientation angles. Each parameter of the limb geometry is found on the left side (see Table 2 for nomenclature explanation). The central vertical line represents the intact, left side as the physiological template. Each animal's right knee is represented by a dot. Thus, for each limb alignment parameter, 22 figures are found around the central vertical line. The dotted lines to the left and right represent the thresholds for significant limb alignment side-to-side differences. It could be demonstrated that no single animal developed a significant growth disturbance.

individuals without necessarily creating growth disturbances. However, it seems to be mandatory to use a well-designed surgical technique that follows those criteria identified to prevent growth disturbances in humans.

Recently, there has been an increased interest in early, aggressive operative management of ACL injuries to restore stability in skeletally immature patients.[3] This interest arose from an increasing number of publications reporting a high rate of secondary meniscal tears during conservative treatment.[1,3,17,18] According to the recent literature, adolescents with an age of 14 years (girls) or 15 years (boys) may undergo ACL reconstruction as in adults. Patients 12 years and older should currently be treated in a "physeal respecting" way.[3] However, the indications for a transphyseal ACL reconstruction in very young patients (ages 8-12 years) with a high remaining growth capacity are still controversial. Controversy exists as to whether the benefits of early ACL reconstruction to prevent secondary meniscal tears outweigh the risk of possible growth arrest.[3] According to a recent survey of the Herodicus Society and the ACL Study Group, 58% of the orthopaedic surgeons would not operate on an 8-year-old boy with an intraligamentous rupture of the ACL because they fear growth disturbances.[14] In a 13-year-old boy, still 51% of the surgeons would choose an initial nonoperative treatment.[14]

Previous animal models of ACL reconstruction during growth aimed to define factors that create growth disturbances due to iatrogenic physeal damage. They also proved that animal models of ACL reconstruction during growth are adequate models to potentially create growth disturbances (Table 1).[5,7,10,19,22,25] Our model was different. We chose a surgical technique that followed certain criteria known to be important in preventing growth disturbances. This is one of the strengths of the present study. Another strength of our model is that the remaining growth capacity of the sheep resembled that of a 9- to 12-year-old human, which sets the focus on the age of clinical interest.

There are some weaknesses in the present study. The ability to extrapolate the results of animal studies to humans is limited, even if the sheep knee is known to approximate the human knee very closely.[12,26] Another weakness is that we did not directly study the growth plate of these animals, as focal areas of physeal interruption may occur in the absence of perceived growth disturbances. Such a visualization could have been performed by fat-suppressed gradient echo scans, which are known to be physeal-sensitive.[6] We also did not assess torsion and rotation of the tibia and femur. Rotational abnormalities have been shown in a previous canine model.[5]

CONCLUSION

No growth disturbances were found in our sheep study model after a transphyseal ACL reconstruction. The data of the present study support the trend toward an early transphyseal ACL reconstruction, even in very young individuals with wide-open physes. This can be performed as long as certain important surgical criteria are followed. This large-animal study strengthens the position of the proponents of early operative treatment of an ACL rupture, even in young patients.

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