Outcomes of Anterior Cruciate Ligament Reconstruction Using Biologic Augmentation in Patients 21 Years of Age and Younger

Anthony S. Berdis, D.O., Kodi Veale, P.A.-C., and Paul R. Fleissner Jr., M.D.

Purpose: To report on the outcomes of a subset of patients ≤21 years of age after anterior cruciate ligament (ACL) reconstruction coupled with biologic augmentation using platelet-rich plasma (PRP) and a porous collagen carrier. **Methods:** A cohort of patients was retrospectively reviewed after ACL reconstruction with hamstring autograft tendon. All reconstructive surgeries combined biologic augmentation in which the ACL graft was coupled with PRP contained within porous collagen membrane. Patients were included if they maintained a minimum follow-up period of 24 months. Outcomes were assessed through patient-reported questionnaires and physical examination in the clinical setting. Patient-reported outcomes including International Knee Documentation Committee (IKDC), Lysholm, Tegner, and Single Assessment Numeric Evaluation (SANE) scores were collected. ACL stability was evaluated using Lachman and KT-1000 testing. Patients were also evaluated for return to play at the same level of competition, family history of ACL injury, and time to complete rehabilitation. **Results:** A total of 194 patients were initially eligible; 143 (74%) patients with 151 knees were ultimately evaluated. The average patient age was 16 years; 79 patients were female and 64 were male. Follow-up duration averaged 52 months. IKDC and Lysholm scores averaged 91 and 91; the average SANE score was 94. The KT-1000 side-to-side difference averaged 1.2 mm. The average time to complete physical therapy was 22 weeks, and 132 patients (92%) returned to their preinjury level of competition. There were 23 cases of contralateral ACL injury (15%) and 7 cases of ACL reinjury necessitating revision surgery (5%). **Conclusions:** Biologic augmentation with hamstring autograft in ACL reconstruction shows a decreased rate of second ACL injury, specifically with regard to ACL revision surgery. The patients in this study also show higher return to preinjury level of competition at a faster rate than other studies have shown. **Level of Evidence:** Level IV, Therapeutic Case Series.

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Anterior cruciate ligament (ACL) injuries are commonly encountered in the practice of sports medicine, with current literature estimating an incidence of 100,000 to 200,000 cases per year.[1,2] Particularly among pediatric and adolescent populations, these injuries are becoming more prevalent[3]: recent reports have suggested that the numbers are steadily growing, with an incidence of 0.1 to 2.4 patients per 10,000 annually.[4]

A multitude of options exist for the young patient needing ACL reconstruction (ACLR). These include transphyseal versus physeal sparing approaches and graft options such as hamstring autograft, quadriceps tendon autograft, and soft-tissue allograft.[5] Regardless of graft and technique, reports have shown increased risks of graft failure in youth populations compared with their adult counterparts. In general, younger age, a family history of ACL injury, return to activity that includes excessive pivoting (e.g., soccer), accelerated return to activity, and allograft usage have all been associated with increased rates of ACL graft failure after reconstruction.[6] Graft failure after successful ACLR in patients ≤21 years of age approaches rates as high as 25% in some studies.[1,3] Although rupture of the reconstructed ligament is an obvious concern, subsequent injury to the ACL of the contralateral knee is also recognized.

The use of biologic agents, such as platelet-derived growth factors and stem cells, remains an area of interest as surgeons explore new means to improve

From the Department of Graduate Medical Education, Aultman Hospital (A.S.B.), Canton, Ohio, U.S.A.; and the Crystal Clinic Orthopaedic Center, Bell Chapter of the Hawkins Foundation (K.V., P.R.F.), Akron, Ohio, U.S.A.

The authors report the following potential conflicts of interest or sources of funding: P.R.F. is a consultant for Exactech. Full ICMJE author disclosure forms are available for this article online, as supplementary material.

Received January 4, 2019; accepted May 23, 2019.

Address correspondence to Anthony S. Berdis, D.O., Aultman Hospital, 2600 Sixth St SW, Canton, OH 44710, U.S.A. E-mail: asberdis@gmail.com

0749-8063/1911/$36.00

https://doi.org/10.1016/j.arthro.2019.05.047

healing.[7] Platelet-rich plasma (PRP) is a biologic agent that has received significant attention. Although it is known that patients may show differing levels of platelets, often varying by time of day, all patients experience up to a 4-fold increase in platelet concentration with appropriate processing.[8-10] Some animal studies have shown increased cellular density and neovascularization when PRP is injected in a ligamentous graft at the time of implantation, ultimately leading to improved biomechanical properties.[7,11-13] In cases of ACLR, this adjunct is thought to enhance the overall integrity of the reconstructed ligament.[14] Although a certain amount of fibrin clot forms in vivo after postsurgical trauma, concentrating specific growth factors that are found within a clot (e.g., PRP) may have unrealized potential. Plasmin, which is also found with increased intra-articular concentrations after athletic or postsurgical trauma, has been shown to degrade fibrin and may prevent effective delivery of beneficial growth factors.[15] With this in mind, collagen scaffolds represent an intriguing adjunct, as soluble collagen can slow plasmin-mediated degradation of fibrin.[16]

Numerous studies in the medical literature have analyzed outcomes after ACLR, but similar reports specifically focusing on pediatric and adolescent patients are sparse. The purpose of this retrospective case series is to report on the outcomes of a subset of patients ≤21 years of age after ACL reconstruction coupled with biologic augmentation using PRP and a porous collagen carrier. We hypothesized that these patients would ultimately show improved recovery with a lower incidence of postoperative failure, especially compared with the outcomes of similar reports that did not use supplemental biologic augmentation.

Methods

Institutional review board approval was obtained. Patients sustaining an ACL injury requiring ligament reconstruction were seen in the office by the attending surgeon (P.R.F.). ACLR was scheduled, with all included patients undergoing surgical intervention from August 2010 to December 2015. Patients were included in this study if they were ≤21 years of age, successfully completed physical therapy, and answered International Knee Documentation Committee (IKDC), Lysholm, Tegner, and Single Assessment Numeric Evaluation (SANE) questionnaires. They also answered whether they had sustained an ipsilateral or contralateral ACL injury since their initial ACLR, whether they had a positive family history for ACL injury, whether they returned to the same sports after ACLR that they played previously (and if so, what sports), and whether they had any additional surgery on the reconstructed knee since the ACLR. Patients were excluded if they had undergone previous ACLR or sustained a multiple ligamentous injury (with the exception of an medial collateral ligament injury).

All patients received standard femoral nerve regional anesthesia with general anesthetic on the day of surgery. Typical arthroscopic examination and evaluation were performed on each patient, during which the quality of the cartilage of both the patellofemoral joint and medial/lateral tibial-femoral joint spaces, quality of the medial and lateral menisci, and integrity of the cruciate ligaments were evaluated. When meniscal injury requiring repair was noted, repair was carried out using an all-inside system.

In all patients, after a complete tear of the ACL was identified, blood was obtained from one of the patient's antecubital veins by the covering anesthesiologist. The blood was centrifuged and prepared for both PRP and platelet-poor plasma injections later in the procedure.

After gracilis and semitendinosus tendons were harvested from the ipsilateral leg, each patient underwent ACLR with hamstring autograft by the attending surgeon (P.R.F.), using a standard transphyseal technique. To prepare the graft for implementation, a suspensory button was secured to the folded ends of the semitendinosus graft. A porous bovine collagen carrier (Tenomend; Collagen Matrix, Ramsey, NJ), chemically and mechanically processed to produce a porous and pure type I collagen, was then cut to fit the semitendinosus graft. The PRP was then returned to the sterile field via a closed tubing system (Exactech, Gainesville, FL), and 1 to 2 mL PRP combined with thrombin powder (Recothrom, Mallinckrodt Pharmaceuticals; reconstituted with calcium chloride) was used to saturate the collagen carrier. The carrier was circumferentially placed around the semitendinosus graft, and 3-0 Vicryl suture was used to secure the carrier into place with a running stitch. The gracilis tendon was folded over the semitendinosus/carrier construct and similarly sewn into place using 3-0 Vicryl suture.

The graft was pulled through the tibial tunnel using a suture loop and up through the femoral tunnel, engaging the suspensory button into place along the lateral femoral cortex. An appropriately sized, cannulated interference screw was passed over a guide wire to secure the tibial insertion of the graft into position. A final diagnostic evaluation was completed with the arthroscope, ensuring appropriate graft position and the lack of femoral wall impingement (Fig 1). A spinal needle was then fed into the tibial tunnel, through the cannulated screw, and into the graft, coming to rest in the femoral tunnel. The knee was drained of arthroscopic fluid, and the needle was partially withdrawn to inject the remaining 8 to 9 mL PRP with thrombin into the femoral and tibial tunnels. All instrumentation was withdrawn from the knee, and the platelet-poor plasma was injected near the origin of the harvested hamstring tendons using the spinal needle.

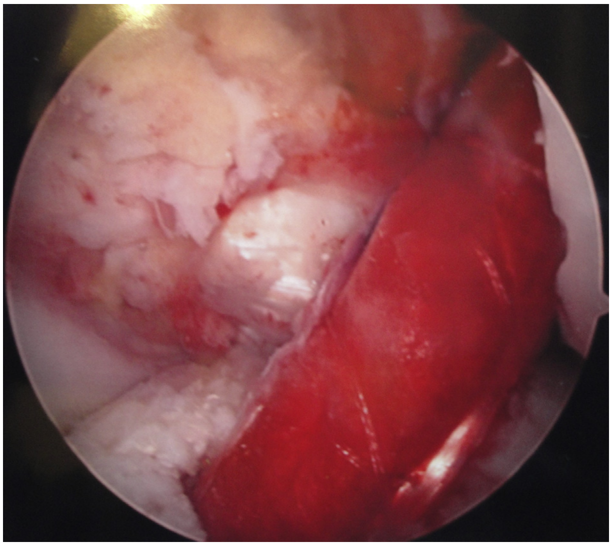

Fig 1. Intraoperative arthroscopic photograph of a left knee from a standard anterolateral viewing portal demonstrating final anterior cruciate ligament graft placement. An overlying porous collagen carrier has been sutured to circumferentially cover the hamstring autograft, and platelet-rich plasma has been injected into the graft.

Postoperatively, the patient was placed into a cryotherapy cuff and hinged knee brace that was locked in extension. The patient was permitted to bear weight as tolerated on the operative extremity with the brace locked in extension. At 6 days postoperatively, the patient was seen in the office for initial postoperative evaluation. At this point, the brace was unlocked, and the patient began physical rehabilitation following the Multicenter Orthopaedic Outcomes Network (MOON) protocol.[17]

The rehabilitation protocol developed by the MOON study group includes a 5-phase rehabilitation that progresses based on the patient's ability to perform specific tasks. Patients were tested with single-leg hop, triple hop, crossover hop, and 6-m timed hop. Results had to score within 85% of the contralateral leg to pass. Deceleration shuttle testing was also performed. Patients had to have no functional complaints and perform testing with confidence when running, cutting, and jumping to progress.

Serial postoperative Lachman testing was performed bilaterally, beginning at 6 weeks. This was again performed at 3 and 6 months and at the final follow-up appointment by 2 of the principal investigators. All patients were tested at final follow-up for pivot shift phenomenon and evaluated with a KT-1000 arthrometer. Patients were evaluated independently of the operating surgeon by a physician assistant (K.V.) with experience in the use of a KT-1000 machine as well as Lachman testing. Each patient completed the MOON protocol and passed functional testing before the final follow-up appointment. At that point, each patient was cleared for return to activities without restriction. Bracing was discontinued once the patient showed a normal gait pattern with appropriate neuromuscular control of the operative leg. Mandatory bracing was not used in any patient.

We did not include a power analysis because of the lack of a control group. If we had included one, we determined that the number of required patients would have been 73.

Results

There were 194 patients initially eligible for this study (Table 1); 143 patients (74%; 79 female and 64 male) with 151 knees (75 left and 76 right; 8 patients sustained bilateral knee injuries) met the above inclusion criteria and completed follow-up questionnaires. A subset of 101 patients (109 knees) were able to return for KT-1000 and Lachman testing in addition to answering the questionnaires. The remaining 42 patients did not return for physical testing because of travel restraints, but they were able to answer questions on the phone and return the questionnaires by mail. Questionnaires were completed in the last 6 months, and all patients were asked to contact the authors immediately if a new injury occurred. Fifty-seven of the knees involved had associated meniscal surgery with the initial procedure, including 19 medial meniscal repairs, 2 partial medial meniscectomies, 26 lateral meniscal repairs, and 21 partial lateral meniscectomies. The average graft size was 9 mm, range 8 to 11 mm; this diameter was determined before the addition of the collagen scaffold.

The mean patient age was 16 years, range 8 to 21. The average time to complete physical therapy was 22 weeks, range 12 to 41 weeks (Table 2). Upon completion of physical therapy, 132 patients (92%) returned to their preinjury level of activity. The average total follow-up duration was 52 months, range 25 to 94 months. Thirty-two patients (21%) had a family history positive for ACL tears.

Table 1. Patient Characteristics (N = 143, 151 Knees)

Characteristic	Value
Mean age (yr)	16 (range 8 to 21)
Male	64
Female	79
Right knee	76
Left knee	75
Unilateral ACL reconstruction	135
Bilateral ACL reconstruction	8
Associated meniscal surgery	57
Medial meniscal repair	19
Partial medial meniscectomy	2
Lateral meniscal repair	26
Partial lateral medial meniscectomy	21
Mean graft size (mm)	9 (range 8 to 11)

NOTE. Data are expressed as n unless noted otherwise.
Abbreviation: ACL, anterior cruciate ligament.

Table 2. Functional Scores and Physical Therapy (N = 143, 151 Knees)

Metric	Value
Average duration of physical therapy (wk)	22 (range 12 to 41)
Return to sports activities (%)	98 (141 of 143)
Average follow-up duration (mo)	52 (95% CI 49 to 55)
Mean IKDC score	
Preoperative	44 (95% CI 39 to 49)
Postoperative	91 (95% CI 89 to 93)
P value	<.002
Mean Lysholm score	
Preoperative	55 (95% CI 50 to 60)
Postoperative	91 (95% CI 89 to 93)
P value	<.04
Mean Tegner score	
Level before injury	9
Level returned to	9
Not returned to before-injury level (%)	7.7 (11 of 143)
Returned to same level (%)	89.5 (128 of 143)
Returned to higher level (%)	2.8 (4 of 143)
Mean SANE score	94 (range 60 to 100)

Abbreviations: CI, confidence interval; IKDC, International Knee Documentation Committee; SANE, Single Assessment Numeric Evaluation.

Seven cases (5%) of ipsilateral ACL reinjury occurred that required revision surgery (Table 3), with an average time injury of 17 months. There were 23 contralateral ACL injuries (15%) at an average time of 28 months from the initial surgery.

Multiple patients participated in >1 sport (Table 4); these patients did not feel that they had a single, primary sport. If a patient felt as though they played primarily 1 sport, they were included as a 1-sport athlete.

Lachman testing was 0 to 1 on all patients except for 1 patient, who registered a grade of 2 (Table 5). No patients perceived any difference in their Lachman testing when comparing one knee to the other. KT-1000 testing performed on 101 patients revealed an average difference of 1.2 mm, range 0 to 5, when evaluating the reconstructed knee in comparison to the opposite knee.

Mean IKDC and Lysholm scores were 91 and 91, with ranges of 55 to 100 and 57 to 100, respectively (Table 2). Tegner scoring was the same both preoperatively and postoperatively in 138 of 151 knees; 11 scores were lower postoperatively than preoperatively, whereas 4 scores were higher postoperatively. The mean Tegner score preoperatively was 9, range 5 to 10, whereas the mean postoperative score was 9, range 4 to 10. The average SANE score was 94, range 60 to 100.

Table 3. Additional ACL Surgery (N = 143, 151 Knees)

Category	Value
Patients requiring ACL revision surgery (n)	7 (5%)
Average time to ACL retear (mo)	17 (95% CI 9 to 47)
Patients requiring contralateral ACL surgery (n)	23 (15%)
Average time to contralateral ACL injury (mo)	28 (95% CI 19 to 37)

Abbreviations: ACL, anterior cruciate ligament; CI, confidence interval.

Table 4. Sporting Activity After ACLR (N = 143, 151 Knees)

Category	Value
Patients who continued with sports postsurgery (%)	98 (141 of 143)
Patients returning to sport of injury (%)	92 (132 of 143)
No. of sports participated in after ACLR	
1	102
2	30
3	9
Sports played after ACLR	
Soccer	49
Basketball	39
Football	32
Other (e.g., gymnastics, skiing)	14
Volleyball	13
Softball	11
Baseball	10
Wrestling	5
Rugby	2

NOTE. Data are expressed as n unless noted otherwise.
Abbreviation: ACLR, anterior cruciate ligament reconstruction.

Discussion

Graft failure after successful ACLR in pediatric and adolescent populations is reported to be as high as 25%.[1] In this study, we found that graft failure was 5%, with a 15% contralateral ACL injury rate. Although rupture of the reconstructed ligament is an obvious concern, injury to the ACL of the contralateral knee is also a recognized complication. Webster et al.[6] examined a cohort of patients <20 years of age at the time of ACLR with hamstring autograft. They identified an overall rate of 35% when assessing for second ACL injuries. This included an ipsilateral graft failure rate of 18% at a mean of 1.8 years after surgery, as well as a rate of 17.7% of contralateral ACL injury at an average time of 3.7 years from surgery. Similarly, the Kaiser Permanente ACL registry identified an ACL revision rate of 32% in patients <21 years of age while noting that the risk of contralateral ACL injury decreases by as much as 4% every year that age increases.[6,18] A major difference between this study and the studies in Webster's cohort and the Kaiser Permanente registry is the use of PRP and a collagen carrier. Although the

Table 5. KT-1000 and Lachman Testing (n = 101, 109 Knees)

Test	Value
KT-1000 at last follow-up	1.2 (range 0 to 5)
Lachman grade at last follow-up	0 to 1 (all but 1 patient)
0 to 1	100
2	1

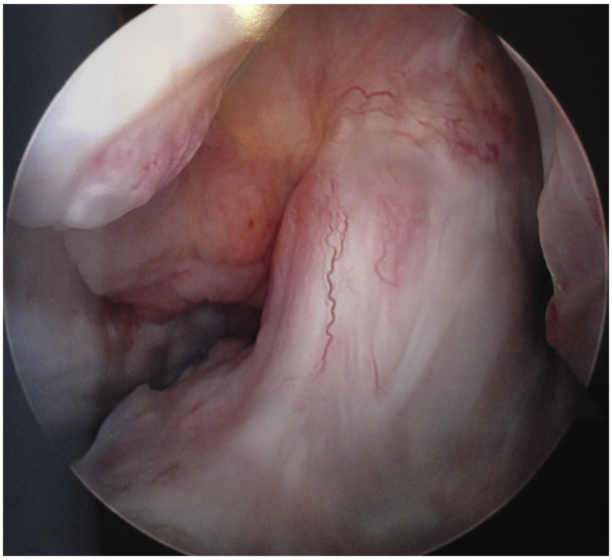

Fig 2. The same patient as in Fig 1, 7 months after the initial procedure. Patient was reevaluated with diagnostic and operative arthroscopy after sustaining a new injury while playing basketball. The reconstructed ACL has fully incorporated, with demonstrated ligamentization and neovascularization, again visualized from a standard anterolateral viewing portal.

incidence of contralateral injuries in this report are similar to those in the above studies, our reported incidence of revision surgery is much lower.

PRP has received much attention recently in sports medicine surgery, as it contains many growth factors that may enhance graft maturation and bony ingrowth.[19,20] This has prompted others to explore its capabilities with regard to improving both the duration and quality of the healing processes.[12,14,19-26] Weiler et al.[14] showed that the application of 1 growth factor contained within PRP, platelet-derived growth factor, can alter the natural history of graft remodeling, improving its tensile strength and resistance, increasing its maturation rate, and improving overall collagen quality. Radice et al.[23] showed a 48% reduction in the time to graft maturation by using PRP-soaked Gelfoam to coat the graft in their ACL reconstructions and magnetic resonance imaging to evaluate healing. In our study, it was hypothesized that by using a similar collagen carrier, the clot of growth factors that formed after PRP injection would remain in place to maintain an optimal biologic environment during ACL graft incorporation.[19] In 1 of our patients, a repeat diagnostic arthroscopy was performed 7 months after the index procedure after the patient sustained a new injury while playing basketball. The reconstructed ACL was found to be fully incorporated, with excellent evidence of neovascularization, lending support to this theory (Fig 2).

Of 143 patients in this review, 132 returned to competitive sports at the same level of competition as before their injury. Some reports have suggested withholding the pediatric patient from competitive activity for 18 to 24 months after ACL reconstruction with a hamstring autograft, which seems to be somewhat impractical.[6,11] Still, we have found that many recommendations call for a minimum period of 6 to 9 months before returning to competition.[5] The patients in this study were able to return to competition at an average of 22 weeks after surgery, with minimal incidence of graft failure, as noted above.

Numerous return-to-play standards are based on reports suggesting that second ACL injury is most common in young patients within the first 2 years postoperatively.[6,11] Paterno et al.[27] showed in their prospective case-control study that, when returning to sport within 1 year after ACLR, young patients (average age of 16.3 years) were 15 times more likely to sustain an additional ACL injury than healthy controls with no history of ligamentous injury. This is perhaps supported by the time frames associated with healing and incorporation of the graft into the native tissue after surgical reconstruction. Pauzenberger et al.[28,29] performed a systematic review to particularly examine the process of hamstring tendon autograft incorporation after ACLR. Their results suggest that hamstring tendon autograft undergoes a delayed remodeling phase, typically occurring between 12 and 24 months after surgery. By comparison, patellar tendon autografts were found to undergo the same remodeling phase between 6 and 12 months postoperatively. These are often the time frames when athletes are attempting to return to their respective sports and activity levels, and it is during this remodeling phase that the reconstructed ACL has been shown to be the weakest and most susceptible to a repeat injury.

There were 7 revision surgeries in our study. The earliest of these occurred at 4 months (2 patients) and 6 months (2 patients) after the index ACLR. The remaining 3 cases of subsequent graft rupture occurred at 30, 32, and 54 months after the initial procedure. These latter 3 cases are well beyond the time point required for proper graft incorporation into bone. In one of these cases, the patient returned to competitive gymnastics at the collegiate level without problems; the second ACL injury occurred almost 6 years after initial ACLR when her high-heeled shoe became stuck in a gravel parking lot and she suffered a twisting, varus injury to the knee.

All but 11 of the patients cited in this review returned to their previous level of activity (92%). Of those who indicated that they did not return to the same sport or level of activity, 4 were high school athletes that chose not to continue competing at the collegiate level; it is unknown whether they would have had the desire or ability to compete at the collegiate level in the absence of an ACL injury. One of the patients was 21 years of age at the time of his injury, which was sustained while playing backyard football.

Limitations

This study does contain recognized limitations. Our incidence of second ACL injury may be underrepresented. Some of those with second ACL injury may have sought second opinions elsewhere, been lost to follow-up, had less of a desire to respond and share their results, or a combination of the above. Another limitation is the lack of a control group. We believe there are similar populations in the literature, including Webster et al.[6] and Dekker et al.,[3] with which to compare our results and act as controls. Additionally, we acknowledge that although this report is presented as an analysis of midterm outcomes, more long-term follow-up is required to form definitive conclusions. Specifically, this work would be strengthened with a higher-volume analysis performed as part of a randomized controlled trial.

Conclusions

This study using biologic augmentation with hamstring autograft in ACL reconstruction shows a decreased rate of second ACL injury, specifically with regard to ACL revision surgery. The patients in this study also show a higher return to preinjury level of competition at a faster rate than other studies have shown.

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