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Module 5_PartA

PICO: In middle-aged, active individuals status post anterior cruciate ligament reconstruction (ACL-R), does an allograft or autograft lead to better return to premorbid activity levels?

Introduction

Anterior cruciate ligament (ACL) ruptures are one of the most common injuries in active and athletic populations.[1,2,3] Disruption of the ACL can lead to significant functional impairment. ACL reconstruction (ACL-R) is intended to restore knee joint stability, avoid long-term degenerative problems, and improve overall function.[1,4,5] Several authors have suggested that operative management is considered the gold standard for treatment in restoring stability of the ACL-deficient knee in younger patients, but treatment of older individuals with ACL injury is somewhat controversial.[2,5,6,7] Most orthopaedic surgeons are concerned about an increased likelihood of arthrofibrosis in older patients, and that the higher prevalence of articular cartilage defects in this age group might lead to poorer results following surgery.[5] The activity levels of middle-aged individuals (35-54yo) are trending towards a more dynamic and healthier lifestyle, with a prominent rise in recreational athletics.[2] Consequently, these individuals are becoming increasingly unwilling to compromise or modify their activity levels after sustaining an ACL injury.[5,8] Thus, it is important to consider the surgical options available and how this might impact the ability to return to desired activity levels.

Early surgical stabilization is often recommended to return successfully to the same activity level after injury.[3] A variety of graft choices exist among autologous and allograft tissues. Autograft options include bone-patellar tendon-bone (BPTB), double- or quadruple-stranded hamstring tendon, or quadriceps tendon grafts.[6,9] Allograft tissue offers more options, including BPTB, hamstring tendon, tibialis anterior or posterior tendon, Achilles tendon, or fascia lata grafts.[6,9,10] For many years, the reference standard has been considered BPTB autograft[9]; however, allograft tissue is also a very viable option. Autograft tissue has the advantages of no risk of disease transmission, a high success rate, no immunogenic response[9], and faster incorporation and healing.[11] Disadvantages of autografts include donor site morbidity[11], difficulty of graft harvest, additional operating room time, and limits and unpredictability in graft sizes and quality.[9] On the other hand, allograft tissue has the advantages of absence of donor site morbidity, shortened operating

room time, improved cosmesis[10], and greater availability and predictability of graft sizes.[11] Disadvantages of allografts include risk of disease transmission, delayed incorporation time, higher costs[9], and variability in mechanical strength due to secondary sterilization techniques.[10] Overall, graft selection depends on several factors including, but not limited to, surgeon and/or patient preference, age, activity level, and associated ligamentous injuries.[11]

Furthermore, the time frame for recovery may be dependent on patient age and the general incorporation of the graft tissue. General effects of aging influence the healing capacity of all musculoskeletal tissue. These changes include a decrease in blood supply to the tissues, decreases in the number and metabolic activity of reparative cells in the body, and a decreased inflammatory response.[12] All of these factors contribute to a decreased capacity for healing response in the older individual. Additionally, the incorporation of the graft used in an ACL-R is tissue dependent. All grafts undergo a sequential process of healing and ligamentization.[9] Allografts have similar biomechanical properties to autografts, but they demonstrate a slower rate of biologic incorporation and remodeling, and lead to the prolonged presence of an inflammatory response.[13] Thus, graft choice may have an impact on an individual's recovery time following ACL-R.

The purpose of this review is to outline the literature regarding the efficacy of using allograft or autograft tissue in an ACL-R of the middle-aged, active individual in facilitating a better return to premorbid activity levels. Although this is a comparison of surgical interventions, the results of this clinical question may determine the physical therapist's approach to the rehabilitation protocol and plan of care for these individuals.

Summary of the Evidence Review

A review of the literature for a comparison of autograft versus allograft tissue used in ACL-R of this population reveals several studies that vary in outcome measures, inclusion criteria, follow-up time, and rehab protocols. The 8 studies reviewed are all similar in research design, revealing retrospective and prospective cohort or case-control studies. Three studies directly compare results between autograft and allograft tissue[2,14,15], 1 study indirectly compares the two tissues via historical analysis[16], and 4 studies look

individually at specific tissues and provide comparisons to younger patients receiving a similar ACL-R.[5,7,8,17] In the sections that follow, various themes are gathered and discussed between the studies in terms of joint laxity, rehab protocols, selected outcome measurements, and results.

Autograft versus Allograft: Laxity

Joint laxity at the knee is objectively measured in a variety of ways. Clinicians and surgeons often use Lachman testing and KT-1000 arthrometer measurements to determine anterior translation of the tibia on the femur and side-to-side differences. One study that directly compares groups with autograft or allograft tissue does not report laxity as a main outcome.[14] Instead, Ozenci et al. investigate proprioceptive function of the knee following ACL-R, comparing autograft and allograft groups with age-matched controls and a group of subjects with unilateral ACL injuries. The group of unilateral ACL injuries had increased laxity compared to the other groups, but this did not correlate to proprioceptive function.[14] The other 2 studies that directly compare the tissues reveal mixed results in the laxity differences between the autograft and allograft groups. Barrett et al. reported more laxity in the allograft group based on Lachman and KT-1000 testing, but this finding did not reach statistical significance.[2] The investigators stated that allograft tissue takes longer to incorporate into the body than does autograft tissue, using this as a means to explain their finding of increased laxity in the allograft group.[2] Gorschewsky et al. found significant differences between the laxity and re-rupture rate of the allograft group compared to the autograft group at 2- and 6-year follow-up.[15] However, the surgeons in this study used a different sterilization technique for the allografts, involving a combination of irradiation and acetone solvent drying.[15] Therefore, this study is not readily comparable to the other studies that used non-irradiated and fresh-frozen allograft tissues. This is a limitation that will be discussed later in this review.

Kuechle et al. looked at allograft ACL-R in patients over 40yo at 3- and 5-year follow-ups.[16] Most patients had a grade 0 or 1 Lachman test and a KT-1000 side-to-side difference of less than 3mm at all levels of testing, revealing that stability did not seem to degrade over time.[16] Another study compared allograft ACL-R between patients older than

40yo and patients younger than 40yo.[8] These investigators found no significant differences between groups postoperatively in Lachman or KT-1000 measurements.[8] Plancher et al. examined the use of autograft tissue in ACL-R of patients between 40-60yo.[7] Investigators compared preoperative and postoperative Lachman and KT-1000 testing, finding dramatic improvement in joint stability for all subjects.[7] However, there was no control or comparison group in this study. Brandsson et al. do not report the type of graft used in their ACL-R, but objectively they found no significant side-to-side differences in laxity between subjects age 40yo or older and subjects age 20-24yo.[17] Finally, Blyth et al. look at autograft ACL-R in patients over 50yo and compare results to published series in younger patients.[5] A mean difference of 2.7mm was found in KT-1000 side-to-side comparisons in their subjects, but this did not seem to affect return to functional activity.[5] Authors hypothesized that this increase in laxity might be due to the creep of the graft during biological healing and remodeling.[5] Overall, it appears that allograft tissue has the propensity for delayed incorporation, which may result in increased laxity in the ACL-R of this older age group. More direct comparison studies between allograft and autograft ACL-R in this population are needed to ascertain this statement.

Autograft versus Allograft: Selected Outcome Measures and Return to Activity

An assortment of outcome measurements is used across the studies, including the Lysholm Knee Scoring Scale, Tegner Activity Scale, and International Knee Documentation Committee evaluation form (IKDC). The IKDC has multiple components that may be administered separately, including categories for subjective assessment, symptoms, range of motion, evaluation of the ligament, compartmental findings, and symptoms at the donor site.[7] According to this scale, knees are graded as follows: A-normal, B-nearly normal, C-abnormal, or D-severely abnormal.[7] The IKDC also classifies activities according to level of difficulty: Class I includes strenuous sports activities requiring jumping, cutting, and pivoting; Class II involves heavy manual labor and less intensive sports; Class III includes light manual work, jogging, and straight-ahead running; Class IV activities involve only sedentary work and activities of daily living.[7] These measures are valid and reliable, and have been shown to correlate well with activity and function.[18,19]

Barrett et al. studied 63 patients older than 40yo, 38 receiving BPTB allograft and 25 receiving BPTB autograft, with the purpose of determining the better graft source in an older patient population.[2] Of the 8 articles reviewed, this study had the best direct comparison between groups. No significant differences were found in postoperative Lysholm or Tegner scores at each follow-up. IKDC scores indicated that 88% of the allograft group and 84% of the autograft group returned to normal or near-normal levels of activity at 3 months.[2] At 6-month follow-up, 57% of the allograft group and 25% of the autograft group returned to sports (P=.005).[2] Gorschewsky et al. investigated the possibility of achieving comparable results with either surgical method in a non-age-specific cohort of 268 patients.[15] At 6-year follow-up, only 186 patients were available for testing. Lysholm scores were significantly different in mean values between groups (P=.012).[15] As measured by the IKDC, the function of the knee and influence on level of activity was significantly different between groups (P=.023 and P=.022, respectively), possibly due to the increased laxity and high re-rupture rate in the allograft group.[15] These 2 studies are difficult to compare directly because of the unknown age of subjects and use of different sterilization techniques in allograft preparation in the latter study. Both sets of investigators, however, are proponents of operative management and state that both allograft and autograft patients have shown the potential to return to full sport or pre-injury activity levels following ACL-R.[2,15]

Plancher et al. and Kuechle et al. evaluated subjective, objective, and functional results of autograft ACL-R and allograft ACL-R, respectively.[7,16] These 2 studies present similar sample demographics, with ages ranging between 40 and 60yo and comparable mechanisms of injury amongst subjects.[7,16] Lysholm scores improved to a mean of 94 in the autograft study, whereas they improved to a mean of 89.7 in the allograft study.[7,16] Kuechle et al. found that 45% of their patients regained pre-injury activity levels and 36% reduced their activity by 1 level (according to IKDC classification), mostly because they chose to participate in safer, lower level activities postoperatively.[16] Additionally, 79% of these subjects were found to have an IKDC grade of A or B, indicating normal or nearly normal knee function.[16] Plancher et al. indicated that 92% of their autograft cohort improved postoperatively to an IKDC grade of A or B.[7] Almost 80% of these patients were

subjectively able to return to pre-injury sports activities.[7] These studies were not without complication or bias, but they present similar evidence with high rates of stability, return to activity, and patient satisfaction.[7,16]

Barber et al., Blyth et al., and Brandsson et al. compared the use of allograft or autograft tissue between middle-aged patients and younger patients.[8,5,17] Investigators in the former study found significant improvements within each group between preoperative and postoperative Tegner, Lysholm, and IKDC activity scores.[8] No differences were noted between groups in time to return to running or other sport activities.[8] They conclude that, independent of age, allograft ACL-R provides good results based on significant improvements in each age group.[8] Blyth et al. compared autograft ACL-R in patients over 50yo with results from previously published studies in younger patients.[5] Significant improvements were noted from preoperation to postoperation in all Lysholm, IKDC, and Tegner activity scores ($P<.001$).[5] Brandsson et al. compared ACL-R in patients 40yo and older with patients age 20-24yo.[17] Graft type was not specified and surgical technique was poorly described in this study. The only significant difference between groups was found in postoperative Tegner activity scores ($P=.032$). As such, these authors conclude that comparable subjective and objective function can be achieved between middle-aged and younger patients receiving ACL-R.[17] Definitive conclusions cannot be drawn from the latter study because of the lack of graft indication. Overall, it appears that both allograft and autograft ACL-R provide comparable restoration of knee stability and function such that its recipients are able to return to premorbid activity levels.

Rehab Protocols Discussed

A wide range of postoperative rehab protocols was discussed across the studies, varying in both detail and content. Of the 8 articles reviewed, only 6 contained information regarding a protocol. Most of the protocols called for early restoration of full range of motion, initial weight-bearing restrictions, and initiation and progression of closed-chain exercises after the first few weeks.[2,5,8,15,16] Notably, subjects from the Plancher et al. study were taught to use a self-administered rehab program and were discharged with written guidelines, instructions, and an exercise timetable.[7] The authors described their subjects

as highly motivated athletes, but compliance with this protocol is questionable. Varying allowances of return to activity are also noted in 5 of the studies. Barrett et al. allowed both allograft and autograft groups to progress to running at 2-3 months, with return to sports and full activity at 6 months.[2] In their autograft subjects, Plancher et al. indicated that bicycling was resumed at a mean of 4 months, jogging at 9 months, skiing at 10 months, and tennis at 12 months.[7] Subjects in the allograft study by Barber et al. were allowed stationary bicycling at 8 weeks, straight-ahead running at 12 weeks, and return to pivoting sports (with derotational brace) at 5-6 months if adequate strength was regained.[8] Autograft recipients in the Blyth et al. study had no specific time limits set on return to running or sport; pain, swelling, strength, and return of proprioception were the factors guiding return to these activities; however, the mean time to return to running was 8.6 months and return to sports was 10.2 months.[5] Gorschewsky et al. stated that patients with sufficient musculature were allowed light running or skipping at 6 weeks and sport-specific training at 10 weeks. Interestingly, return to original sports under competitive conditions was not permitted before 10-12 months postoperation.[15] Careful attention should be paid to these varying time frames, as a premature return to vigorous activity may result in laxity and instability of the knee, leading to a decreased potential to return to pre-injury activities.

Limitations and Recommendations for the Evidence Base

The ideal study design to assess the outcomes of autografts versus allografts is a randomized controlled trial. However, there are inherent ethical and practical concerns involved with randomizing a patient to possibly receive cadaveric tissue.[6] Therefore, a high-quality prospective comparative study may be the best option. As treatment is nonrandom in such a design, multivariable modeling may be used to control for possible confounding variables, such as age or associated injuries. Other than age, the studies examined in this review did not control well for such confounding variables. Most studies did not have strict inclusion/exclusion criteria, therefore many investigators allowed patients with concomitant injuries to be included.[2,7,16] Barrett et al., Plancher et al., and Kuechle et al. performed additional surgical procedures in some of the subjects, including partial meniscectomies, meniscal repairs, or chondral debridement.[2,7,16] Graft selection

was also not consistent across studies. Most investigators used BPTB allo- or autografts[2,5,7,8,14,15], but Kuechle et al. used freeze-dried fascia lata or Achilles tendon allografts and Brandsson et al. did not report the graft type used.[16,17] Additionally, Gorschewsky et al. used a sterilization technique with their allografts that differed from all other studies, resulting in a large 45% failure rate of the patients receiving allografts.[15] Furthermore, while the various rehab protocols had similar goals, future studies should include a uniform protocol for all patients receiving autograft or allograft. Evidence would be stronger if strict inclusion/exclusion criteria controlled for confounding variables, if sample sizes were larger, and if rehab protocols were uniform and compliance was closely monitored. Only then would a true comparison between allograft and autograft tissue be possible for a population of active, middle-aged individuals in order to answer the question of which graft facilitates a better return to premorbid activity levels.

Conclusion

The present review of available evidence cannot detect a superior graft choice that enables middle-aged individuals to have a better return to pre-injury activity levels. Both grafts seem to restore adequate function and joint stability. It is important to note that many factors influence successful return to activity after ACL-R, including age, fitness level, concomitant injuries, and pre- and postoperative rehabilitation.[20] Overarching themes of this review reveal that operative treatment is better than nonoperative treatment and the results of operative treatment in middle-aged individuals are comparable to that of younger patients, regardless of graft choice. However, due to the slower incorporation of allograft tissue, physical therapists (PTs) need to be aware of this prolonged ligamentization process and the impact this may have on rehabilitation. Patients receiving allograft tissue may feel better sooner with the absence of donor site morbidity; subsequently, they may want to progress through rehab faster, thereby placing more stress on their graft than it is able to handle. The clinician needs to be knowledgeable about the graft choice used in ACL-R in order to help prevent instability or recurrence of injury. Special consideration should be paid to the middle-aged population because of the aforementioned decreased and slower healing capacity. This information provides a solid foundation for the development of a Capstone presentation for first-year PT students. ACL

injuries are very commonly seen in outpatient clinics, and it will be imperative to have baseline knowledge of why graft selection is so important and how this impacts the rehab process. Additionally, information from this review may also be used in the creation of graft- and age-dependent ACL rehabilitation protocols. Further research would need to be conducted on current ACL-rehab concepts, but this combined information would provide an excellent base for the development of such protocols, which may facilitate improved functional outcomes in all ACL-R patients.

References:

1. Escamilla RF, Macleod TD, Wilk KE, Paulos L, Andrews JR. Anterior cruciate ligament strain and tensile forces for weight-bearing and non-weight-bearing exercises: a guide to exercise selection. J Orthop Sports Phys Ther. 2012;42(3):208-20.
2. Barrett G, Stokes D, White M. Anterior cruciate ligament reconstruction in patients older than 40 years: allograft versus autograft patellar tendon. Am J Sports Med. 2005;33(10):1505-12.
3. Lewek MD, Chmielewski TL, Risberg MA, Snyder-Mackler L. Dynamic knee stability after anterior cruciate ligament rupture. Exerc Sport Sci Rev. 2003;31(4):195-200.
4. Poehling GG, Curl WW, Lee CA, Ginn TA, Rushing JT, Naughton MJ, Holden MB, Martin DF, Smith BP. Analysis of outcomes of anterior cruciate ligament repair with 5-year follow-up: allograft versus autograft. Arthroscopy. 2005;21:774-85.
5. Blyth MJ, Gosal HS, Peake WM, Bartlett RJ. Anterior cruciate ligament reconstruction in patients over the age of 50 years: 2- to 8-year follow-up. Knee Surg Sports Traumatol Arthrosc. 2003;11(4):204–211.
6. Carey JL, Dunn WR, Dahm DL, Zeger SL, Spindler KP. A systematic review of anterior cruciate ligament reconstruction with autograft compared with allograft. J Bone Joint Surg Am. 2009;91(9):2242-50.
7. Plancher KD, Steadman JR, Briggs KK, Hutton KS. Reconstruction of the anterior cruciate ligament in patients who are at least 40 years old: A long-term follow-up and outcome study. J Bone Joint Surg Am. 1998;80(2):184-97.
8. Barber FA, Aziz-Jacobo J, Oro FB. Anterior cruciate ligament reconstruction using patellar tendon allograft: an age-dependent outcome evaluation. Arthroscopy. 2010;26(4):488-93.
9. Baer GS, Harner CD. Clinical Outcomes of Allograft Versus Autograft in Anterior Cruciate Ligament Reconstruction. Clinical Journal of Sports Medicine. 2007; 26(4):661-681.
10. Cohen SB, Sekiya JK. Allograft Safety in Anterior Cruciate Ligament Reconstruction. Clinical Journal of Sports Medicine. 2007; 26(4):597-605.

11. Vyas D, Rabuck SJ, Harner CD. Allograft anterior cruciate ligament reconstruction: indications, techniques, and outcomes. J Orthop Sports Phys Ther. 2012;42(3):196-207.
12. Gross M. Effects of aging on musculoskeletal system. [Voicethread]. University of North Carolina at Chapel Hill: Division of Physical Therapy; 2012.
13. Gulotta LV, Rodeo SA. Biology of autograft and allograft healing in anterior cruciate ligament reconstruction. Clin Sports Med. 2007;26(4):509-24.
14. Ozenci AM, Inanmaz E, Ozcanli H, et al. Proprioceptive comparison of allograft and autograft anterior cruciate ligament reconstructions. Knee Surg Sports Traumatol Arthrosc. 2007;15(12):1432-7.
15. Gorschewsky O, Klakow A, Riechert K, Pitzl M, Becker R. Clinical comparison of the Tutoplast allograft and autologous patellar tendon (bone-patellar tendon-bone) for the reconstruction of the anterior cruciate ligament: 2- and 6-year results. Am J Sports Med. 2005;33(8):1202-9.
16. Kuechle DK, Pearson SE, Beach WR, Freeman EL, Pawlowski DF, Whipple TL, Caspari-Dagger RB, Meyers JF. Allograft anterior cruciate ligament reconstruction in patients over 40 years of age. Arthroscopy. 2002;18(8):845-53.
17. Brandsson S, Kartus J, Larsson J, Eriksson BI, Karisson J. A comparison of results in middle-aged and young patients after anterior cruciate ligament reconstruction. Arthroscopy. 2000;16(2):178-82.
18. Higgins LD, Taylor MK, Park D, Ghodadra N, Marchant M, Pietrobon R, Cook C. Reliability and validity of the International Knee Documentation Committee (IKDC) Subjective Knee Form. J Bone Spine. 2007;74(6):594-9.
19. Briggs KK, Lysholm J, Tegner Y, Rodkey WG, Kocher MS, Steadman JR. The reliability, validity, and responsiveness of the Lysholm score and Tegner activity scale for anterior cruciate ligament injuries of the knee: 25 years later. Am J Sports Med. 2009;37(5):890-7.
20. Cohen SB, Yucha DT, Ciccotti MC, Goldstein DT, Ciccotti MA, Ciccotti MG. Factors affecting patient selection of graft type in anterior cruciate ligament reconstruction. Arthroscopy. 2009;25(9):1006-10.