Future Trends In Grafts Used In ACL Reconstruction

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Abstract

Anterior cruciate ligament injury is the commonest sports injury in day to day orthopaedic practice and arthroscopic reconstruction of anterior cruciate ligament is the standard of care. This gold standard procedure has evolved continuously since the time of its inception in terms of technique, implant used for fixation and most importantly the graft used. Each period of time was dominated and fascinated by a particular graft option. Though numerous came into the picture only few stood the test of time. Search for the perfect graft for ACL reconstruction still continues. Ideally it should have adequate biomechanical strength, should be easily available and doesn't cause any harm during harvest or implantation. Today we have the option of autografts, allografts and even synthetic grafts. In the future tissue engineering and gene therapy might play a major role in graft production.

Keywords: Anterior cruciate ligament reconstruction, allograft, synthetic graft

Introduction

History of using tendon grafts for ACL reconstruction started in the early sixties. Kenneth Jones(1) was one of the early surgeons who started using tendon for ACL reconstruction. From then on grafts for ACL reconstruction surgery continued to evolve. Every new source of graft had its own advantages and disadvantages. An ideal graft should be one which is easily available, have the properties similar to the native ACL, get incorporated to the bone easily and don't cause any donor site morbidity. As of now, there is no such graft which can completely reproduce the structural and biological characteristics of native ACL without causing an untoward effect. Today we have the option of autografts, allografts and few synthetic grafts. The failures are not only because of the characteristics of the graft but also due to graft healing in the bone tunnel. The future trend of grafts for ACL reconstruction might not be same as we see today because of on going research like tissue engineering. In this article we reviewed the commonly used grafts at present and the future evolving concepts.

1. Tendon grafts

The usage of tendon grafts as a substitute to ligament is due to the fact that they are anatomically and histologically similar. These connective tissues are made up of bundles of collagenous fibers arranged in parallel, slightly wavy or curved arrays. Twenty percent of their mass is made up of cellular component and the remaining 80% is the extracellular components. Fibrocytes and fibroblast comprise the cellular component. 80% of their mass is water. Collagen fibers make 65 to 80% of the dry mass. Type 1 collagen is the one which is abundant in both with some type 3 collagen. Amount of collagen and the ratio between type 1 and type 3 are the differences between the two. The amount of collagen is more in tendons than the ligaments and the ratio between type 1 and 3 is 99:1 in tendons where as it is 90:10 in case of ligaments. Apart from anatomical and histological similarity the strength and other biomechanical properties should be similar between the tendon and the ligament to be replaced. Noyes et al[2] did a biomechanical testing to test the strength between natural ACL and various grafts after excluding age and disuse related factors. They found that semitendinosus and gracillis had 70 and 49 % of the strength of natural ACL while patellar tendon has 159 to 168 % strength compared with natural ACL.

The bone tendon interface is composed of a tissue called enthesis which is a transitional zone transmitting the stress from bone to tendon and vice versa. Enthesis is of two types(3). The first type is the direct insertion type which is typically seen in ACL, patellar tendon, rotator cuff, Achilles tendon and femoral attachment of MCL. Here there is a gradual transition from tendon to bone. Microscopically the attachment point shows interdigitation of collagen fibers with transition from tendon, unmineralized fibrocartilage, mineralized fibrocartilage and bone. The superficial fibers are inserted into the periosteum and the deep fibers are attached at right angles or tangentially to the bone in the transition zone. The second type is the indirect type observed in tibial attachment of MCL and deltoid insertion in humerus. Here there is no fibrocartlaginous transition and the tendon fibers pass obliquely along the bony surface and inserts at an acute angle into the periosteum. They are connected by Sharpey's fibers(4,5). The healing between tendon and bone in case of ligament reconstruction surgery is slightly different. Here there forms a vascularised granulation tissue in the junction which gets replaced by Sharpey's collagen fibers gradually. The attachment gets further strength when bone grows between the interfaces.

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Patellar tendon, hamstring tendon and quadriceps tendon are the three most commonly used autografts. Even among them there is no single outstandingly performing graft. Each one has its own advantage and disadvantage. In a meta analysis done by Li et all (6) patellar tendon graft had favorable outcome in terms of KT-1000 arthrometer values, negative rates of Lachman test and pivot shift while hamstring tendon graft was better in avoiding anterior knee pain, kneeling pain and extension loss. There was no difference in postoperative graft failure rate.

Bone Patellar tendon bone grafts.

BPTB grafts since the time of Jones evolved into a gold standard for ACL reconstruction in last few decades. Jones(1) made a medial parapatellar incision one inch distal to the patella extending just distal to the tibial tubercle. Then a femoral tunnel was made. The central third of the patellar tendon was incised along with a bloc of bone from the patella. The tibial attachment was left intact and the bone block is fixed to the femoral tunnel. Because the graft was attached to the natural insertion site in tibia the length was small making the femoral tunnel to be more anterior than anatomical. Franke was the first to describe the free patellar tendon graft as we use it today(7). By the nineties free bone patellar tendon bone graft became the standard graft for ACL reconstruction and was commonly used. Advantages of this graft are the mechanical strength and the bone to bone healing which occurs with this graft. Anterior knee pain is the major limiting factor for BPTB graft with a reported incidence of 4 to 60 percent(8, 9). The reason for anterior knee pain can be injury to the infrapatellar branch of saphenous nerve, the inflammatory response that occurs during healing of the donor site and even the shortening of the tendon which occurs after graft harvest. To prevent these complications there were many attempts to modify the graft harvesting technique. Berg and Liu sutured the peritenon and filled the bone harvesting site[10, 11]. But these modifications were not entirely satisfactory as seen in further studies[12, 13]. In order to reduce the injury to infrapatellar branch of saphenous nerve, newer minimally invasive two incision techniques were devised. Other more important aspect of concern in this graft is regaining the original strength in the donor site. There are many MRI and ultrasound based studies which showed near complete regain of cross-section area after harvest(14-16). But still rupture of patellar tendon does exist. The risk of rupture is high when closing the defect in the middle with undue tension. Also a tight closure can cause necrosis, fibrosis and shortening of the tendon.When excessive patellar bone is harvested or the intraosseous midpatellar and polar vascular channels are damaged patella fracture can occur(17). There are further modifications in the graft harvesting technique to reduce these complications where instead of the middle third medial third was used(18). Proponents of this technique advocate many advantage of this technique over the classic middle third. Graft can be harvested by a single cut, there is no need to approximate the peritenon and the risk of patellar tendon rupture, shortening, patellar fracture and maltracking are reduced. Today patellar tendon grafts are less frequently used when compared to hamstring tendon grafts. But still it is the graft choice when early bone to bone healing is needed; particularly in sports personnel and athletes who need faster recovery. It is also commonly used in revision surgeries and multiligamenous injuries.

Hamstring tendon graft

Hamstring tendon graft is the commonly preferred graft at present because it can be easily harvested, more cosmetic with few donor site complications with same functional outcome when compared to bone patellar bone graft. Though the use of hamstring tendon as graft became popular in recent time its usage started very early. Galeazzi(19) was the first to use them in 1934. He used semitendinosus tendon to reconstruct ACL. The usage was further made popular by many surgeons like Macey, Lindemann, Agustine(20-22). The reason behind the success of this tendon graft is good clinical outcome and lesser donor site morbidities. Hamstring tendon regenerates after harvest but the time it takes to regenerate and the strength of the newly formed tendon is not clear yet. Careful repair of the facial layer is needed so that the space between layer 1 and 2 in the knee provides a tubular compartment for the tendon to regenerate from the tip of the muscle. This is akin to the nerve regeneration within the endoneurium. Injury to infrapatellar branch of saphenous nerve is a commonly reported complication after the harvest of hamstring tendon graft. Sgaglione(23) et al has reported this complication in up to 70% of the cases. Making an oblique incision instead of the usual vertical incision reduced its incidence(24). De Padua et al (25) had shown that harvesting semitendinosis alone reduces the incidence of nerve injury

Since bone to tendon healing takes longer time rehabilitation after its usage is prolonged. To enhance the incorporation of hamstring tendon people are injecting platelet rich plasma into the tunnels before fixing the hamstring grafts(26). Platelet rich plasma which is supposed to contain numerous growth factors will enhance the bone to tendon healing. But there is no clear cut evidence for this till now. Weakness of knee flexion is also a concern after hamstring tendon graft harvest. However Lipscomb et al(27) had shown that harvesting the both tendons does not affect the knee flexors strength

When compared to patellar tendon graft which has a bone plug, hamstring tendon grafts are known to cause more tunnel widening. L'Insalta et al(28) in their study of 60 patients who underwent ACL reconstruction observed a significantly increased tunnel widening in the group of patients with hamstring tendon graft compared with the other group of patellar tendon grafts. But it doesn't seem to affect the clinical outcome; although it might cause problems during a revision procedure. In a study done by Clatworthy et al(29) comparing the hamstring tendon graft with the patellar tendon graft there was no significant difference in outcome even though tunnel widening was significantly more in the hamstring tendon group.

Quadriceps tendon graft

Quadriceps tendon graft usage was first reported by Fulkerson and Langeland(30) in 1995. Gradually its usage started to increase. But still today it is the least commonly used tendon autograft for ACL reconstruction. The ultimate tensile strength of this graft is more than the native ACL and that of patellar tendon graft(31). It has been shown in a MRI study that a 10mm central strip of quadriceps tendon has 88 percent more volume than a 10mm central strip of patellar tendon(32). There are evidences that volume of the graft directly correlates with the structural properties of the incorporated graft, and also an increased failure rate with decreased graft size(33-34). Similar to patellar tendon graft the major problem with this type of graft is the donor site morbidities like pain and patella fracture. Patella fracture remains a possibility after this graft harvest. In order to reduce this complication people have modified the graft harvesting technique. Quadriceps tendon graft without the bone plug was tried and found to give comparable results(35). But the bone to bone healing which this grafts provide will be lost and the length of the graft will be reduced. The natural insertion of this tendon into the patella is not in the middle but slightly lateralized. So if we go by the centre of the patellar tendon then the bone plug in the patella will be more lateral. According to Scully et al(36) harvesting this bone plug from a slightly lateral portion of patella will predispose to fractures. So they devised a technique to medialize the graft harvest centering over to patella to obtain a bone plug from the middle of the patella. Despite improved harvesting techniques quadriceps graft is less commonly used because of the donor site morbidities. But it provides a valuable option when the other two more commonly used tendons are not available for some reason

2. Allograft

Rise of the allograft occurred in order to reduce the donor site morbidity, reduce postoperative pain and operative time. Eugene Bircher(37) was the first to use this in 1929. He used tendons harvested from kangaroo as an augment or a sole graft. Following this there were few others who used xenografts after which it became unpopular. Then was the time of allografts from human cadavers. Achilles tendon, tibialis anterior, tibialis posterior, hamstrings and patellar tendon were the major allografts harvested from cadavers for ligament reconstruction. But the increase in parenteral viral infection led to its unpopularity in the nineties. The sterilization processes like high dose radiation and ethylene glycol available during those periods affected the mechanical properties of the graft. Many studies have been published which demonstrated the deleterious effect of irradiation and ethelene oxide on allograft(38-39). Improved sterilization techniques and screening techniques revived the allograft in recent times. Data suggests that in 2002 an approximate one million musculoskeletal allografts were used in United States alone as against only 350,000 were used in 1990(40). The Bio Cleanse tissue sterilization system(41) is a recently available system which doesn't affect the mechanical properties of the allograft. It is combination of mechanical and chemical techniques. The graft is subjected to an oscillating positive and negative pressure and treated with chemical agents like detergents and sterilants. This process removes the blood and lipids and destroys the microorganisms. The graft is repeatedly rinsed when the debris and the residual chemicals were removed. Non irradiated grafts are being favored over irradiated grafts in recent times. Prodromoset al(42) did a meta analysis and found that irradiated grafts have an abnormal stability rate in comparison to non irradiated grafts. Apart from transmission of infection from donor to the reciepient, bacterial contamination while processing and preserving these allografts was also a concern. But Greenberg et al[43] showed there was no increased risk of infection with the use of allograft compared with autograft in primary anterior cruciate ligament reconstruction. Most important problem with allograft is slow incorporation of the allograft tissue to bone and decreased failure load till it gets incorporated into the host. Many animal studies and MRI studies in humans have demonstrated this(44-46). Immunogenic reaction of the host to the graft tissue is one more possible complication. Literature evidence regarding the outcome and revision rates of allograft was not always uniform. In a meta-analysis done by Yao et al(47) there was no significant difference in patient reported outcomes scores, range of motion or the tests for laxity between BPTB autograft and allograft. But the revision rates were significantly higher in the allograft groups. Mariscalco et al(48) did a meta-analysis and compared non irradiated allografts with autografts and found no difference between the two in terms of graft failure rates, postoperative laxity and patient reported outcome scores. However allografts are not routinely used because of the cost and availability. Allograft could be the answer when the donor site morbidities and operative time have to be reduced. Improved harvest and storage techniques will increase the availability of the allografts in future

3. Synthetic grafts

Further in line are the synthetic grafts. Synthetic graft is an artificial graft prepared for two purposes. They can either act as the sole graft scaffold over which fibrous tissues develop to provide the stability as that of the native ACL. Or it can be used as a load sharer until the autograft tissue heals and take over the role. To perform this synthetic graft should be chemically stable, biocompatible, should not contain harmful additives, should not be hygroscopic and should contain pores for fibroblasts ingrowths. Above all they should have the physical characters of plasticity, stiffness, strength and traction resistance similar to the original ligament. The drawbacks associated with today's synthetics are adverse immunological reaction, debris dispersion, failure of ligamentization process, breakage, synovitis and chronic effusion. Synthetics made of carbon were the first to enter the market. Jenkins et al(49) developed a carbon made synthetic ligament in 1977. It was initially employed for tendon suturing and later extended to knee ligament reconstruction surgeries. Dandy et al(50) were the first to introduce synthetic grafts in ACL reconstruction. His graft was also made of carbon fibers. Initially these carbon made synthetic grafts were received well, but later they went into disrepute because of early failure due to incompetency to resist torsion forces, inflammatory synovitis and carbon deposition in liver. Came next was the graft made of single strand of polytetraflouroethelene wounded into multiple loops(PTFE/ Gore-tex). Initially this was approved by the US government to be used in cases with failed autografts. It was perceived as the complete graft because of its tensile strength of 5300N, greatest of all synthetic grafts manufactured till date(51). But soon later studies found its deficiencies. After some initial encouraging results Woods et al(52) observed worsening knee stability in long term. Similarly Ferkel et al(53) performed a second look arthroscopy 11 months after 21 ACL reconstructions and found partial damage in 6 cases and complete damage in 4 cases. Soon Gore-tex was withdrawn from the market due to higher failure rate and complications like tunnel osteolysis and deposition of the PFTE particles in lymph nodes.Dacron graft made of polyester was one more product of this breed. It was made up of polyester and had an 8mm sleeve of loosely woven velour and a central core of four tightly woven tapes with a mean strength of 3631N(54). It was first used in acromio-clavicular injuries and later in ACL reconstruction. But this too failed in the long run due to high failure rates.The augmentation concept of synthetics was first given by John Kennedy in 1975 when he introduced a polypropylene ribbon for augmenting the autograft.51 This concept tried providing a support for the autografts until the healing becomes complete. The Leeds-Keio ligament(55) or the LK ligament developed in 1982 with the collaboration of Leeds university of UK and Keio university of Japan met with little success. It was made up of woven polyester fibers in tubular bundle and measured 10 mm in diameter. It acted as a scaffold and induced tissue growth. Porous coating over it allowed the tissue to grow in and form a new ligament. This too failed after it made an early impact. Murray and Macnicol(56) made a long term follow up of 10 to 16 years following ACL reconstruction with LK ligament and found a high failure rate of 28 percent and increased degenerative changes compared with the opposite side.

However the most successful of all the synthetic grafts was the Ligament Advanced Reinforcement system (LARS ligament) made up of polyethylene terephthalate(57). This also acted as a scaffold over which tissue in growth occurs. Its short term follow up showed encouraging results but the long term results are still awaited. Liu et al(58) retrospectively made a comparison between LARS and four strands hamstring tendon autografts and observed excellent functional outcomes and higher knee stability in LARS. Polyethylene teraphthalate materials were most commonly used to augment the tissue grafts. Despite repeated failures synthetic grafts continues to evolve over time and manufacturers kept pulling out a new product out of their sleeve every now and then. Confidence over the synthetics is still maintained because of the few studies which showed promising results(55, 57-58).

4. Tissue engineered grafts

This could be the future of ligament reconstruction surgeries. This technology was originally devised to repair skin, cartilage and bones but could be extended to ligaments in the near future. Tissue engineering is basically a combination of engineering, molecular biology and medical knowledge to create biological tissues or organ in vitro. Here organ or tissue growth is done in vitro over a scaffold(59). It is made by nanotechnology which produces a biomimetic structure to replicate the native architecture of the tendon extracellular matrix. Extracellular matrix of the tendon is made up of interconnected porous microstructure composed of collagen fibers. This scaffold provides the structural support over which cells grows due to chemical and mechanical stimulus. The scaffold used will be biodegradable and biocompatible along with the desired biomechanical properties. Both natural and synthetic scaffolds are being used. Collagen, silk, hyaluronic acid are examples of naturally available scaffolds while Dacron polyester, polyglycolic acid and polylactic acid are examples of synthetic scaffolds. Once the engineered graft is taken up the scaffold will gradually degrade and the cells should take over their place. Cells employed here can be mesenchymal stem cells or a tenocyte. In a study done by Kryger et al(60) tenocytes, bone marrow derived mesenchymal stem cells, adipose tissue derived mesenchymal stem cells and tendon sheath fibroblast were seeded into acellularised tendon tissue and implanted in vivo into a flexor tendon defect. After 6 weeks histological analysis revealed viable cells in all four types. But the mechanical property of each type was not analyzed.Best cells to be employed for engineering a tendon is still not clear. Currently no case of ACL was operated with a tissue engineered graft as this is a newly developing technology. Gene therapy will come to play a role in tissue engineered ACL grafts. Currently gene therapy is being researched in repairing tendon injuries(61) and the same can be applicable in ligament injuries. There are two different strategies in gene therapy(62). One is in vivo transfer of the gene within a vector which is then directly applied to the target tissues. Lou et al(63) used BMP-12 gene to treat complete tendon laceration in chicken model and found a two fold increase in tensile strength and stiffness of the repaired tendon. The disadvantage of this strategy is that there is always a possibility of transfecting the cells adjacent to the target tissue. Another disadvantage is the development of immune response to the vector. The second strategy involves harvesting the target tissues from the body, trasfecting them with the vector and then allow them to grow in a culture in vitro. Once the tissue gets matured they can be transferred to the target area. This approach seems very promising for ligament reconstruction surgeries. The idea of using stem cells in ligament injuries can become feasible in the near future. Stem cells could be harvested and induced to grow a particular mesenchymal lineage to repair the injured ligament.

Conclusions

Tendon grafts continue to be the commonly used material for ACL reconstruction surgeries. Both autografts and allografts have its own pros and cons. Each surgical case should be individualized and the choice of the graft should be made. Allografts usage continues to grow. In the future with appropriate precautions this might become a major source for ACL reconstruction. Synthetic grafts and tissue engineered grafts are still in the developing phase. The usage of these grafts has a long way to go. Till then autografts and allografts are the choices of graft for ACL reconstruction.

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