

# Rupture and repair of the anterior cruciate ligament

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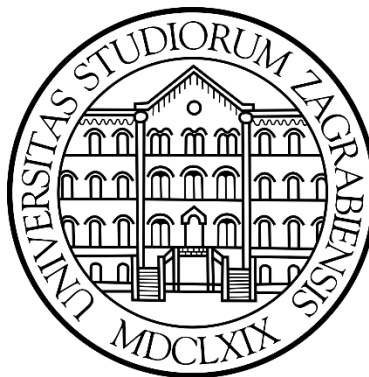
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UNIVERSITY OF ZAGREB  
SCHOOL OF MEDICINE

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# Rupture and Repair of the Anterior Cruciate Ligament



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**Summary:** The human body is constantly in use, being a bipedal species one can forget that for the majority of the time humans are on their feet. This results in a passive use of the locomotor system more specifically the lower limbs. Combined with an active interest in pursuit of sporting endeavours, humans have come to rely heavily on their legs. Through this constant use we are bound to observe injuries, these can be from passive activities such as falls or from sporting accidents. The rupture of the anterior cruciate ligament (ACL) is such an observable injury. Several conclusions can therefore be made epidemiologically speaking to the incidence and prevalence of the injury across the two genders and the age at which the injury is most likely to occur. Finally, there are discernable differences between repair methods. The surgeon and patient have to take into account the benefits a certain approach might have in augmenting the patient's lifestyle. Based on what the patient perceives as best for their lifestyle habits, we can select the method of reconstruction that is more suited to a demographic.

**Sažetak:** Ljudsko tijelo je stalno u pokretu i mi kao bića koja hodamo uspravno možemo lako zaboraviti da većinom vremena provodimo na našim nogama. S obzirom na naš aktivni interes za zdravi život, najčešće kretnje uključuju upravo korištenje donjih ekstremiteta. Stoga, upravo su ozljede donjih ekstremiteta i najčešće ozljede našeg lokomotornog sustava. Ruptura prednjeg križnog ligamenta je jedna od najčešćih ozljeda uopće lokomotornog sustava. Nadalje, na temelju epidemioloških studija, mogu se iznijeti zaključci o incidenciji i prevalenciji te ozljeda na temelju razlike u dobi i spolu pacijenata. Konačno, na temelju tih razlika, može se donijeti i zaključak o načinu liječenja s obzirom na dob, spol te potrebe osoba s ozljedom prednjeg križnog ligament.





## **Introduction**

The purpose of this review is to grasp a better understanding of the components in play regarding ACL rupture and repair. ACL surgery is among the most common sports surgeries, having 100,000 performed each year in the United States alone (39). The strain on the health care system is therefore significant with the mean lifetime cost on society calculated to be around USD \$38,121. However, both the cost and benefit is greater than conservative treatment which was calculated to cost society USD \$88,538. Surgical treatment offers a Quality adjusted life years (QALY) gain of 0.72 (40). Firstly, we need to establish the two types of ACL injury, contact and non-contact. A noncontact mechanism of ACL injury, which will be the main focus of this review, occurs in 70-80% of cases. These injuries mostly occur while landing from a jump, simultaneously cutting or with a sudden deceleration (3). Meanwhile contact (traumatic) injuries are frequently associated with a forceful valgus stress and concomitant injury to the medial meniscus and medial collateral ligament injuries. Important components to consider in assessing an ACL tear is to identify the at risk groups, in doing so thorough research is conducted and conclusions are drawn so that clinicians can further their understanding of the pathogenic cause of the injury and its relation to the patient. Therefore certain risk groups have been established that include gender, age, genetic and anatomic predisposition and even potential hormonal links. Once these associations have been formed we can then begin to discuss how different surgical approaches offer varying degrees of relief for the patient.

## *Gender*

On an anatomic level the difference between genders is clear. Anatomic variances in the female pelvis such as wider protruding iliac wings, transversely oriented obturator foramina and a definite pubic angle are noticeable when compared to the male pelvis, which has a subpubic angle and more erect iliac wings along with a smaller lesser pelvis (1,2). This provides us a functional basis in the way that we can compare the sexes. The resulting transverse obturators cause the angle of inclination in females to be more towards acute (2). Therefore coxa vara is formed in the hip and at the level of the knee, genu valgum. As is widely known the 'position of no return' is that of flexion in the hip joint, knees in valgus and foot pronated (3). The anatomical predisposition to valgus as a neutral position for females is a potential cause to the increased incidence in ACL injury. As observed through previous works, that looked at dynamic knee valgus in 300 female high school athletes. They found that dynamic knee valgus was greater in athletes who suffered ACL injury (13). One study found that compared to males, female basketball athletes sustained 3.79 times more ACL injuries per exposure hour. The risk of injury in both males and females was greater during games than during practices (5,17). This phenomenon of increased female ACL rupture has been seen across many reviews for such injuries. However, the difference in rupture between the two genders seemed to be bigger in athletes who played soccer (11,17). Lending weight to the multifactorial hypothesis of injury that not only nonmodifiable factors but also modifiable factors contribute to ACL rupture. Furthermore, when reviewing the epidemiology of female ACL injuries through various levels of skill ranging from NCAA, Olympic and military service (4,18). These data showed increased risk of sustaining knee injury and an even higher associated risk in ACL tear. Studies have also looked at anthropomorphic differences between female and male ACLs, in which they have

shown that female ACL are disproportional small to their intercondylar notch width at two thirds of the notch height (NW-2/3) (19). The disproportional nature of the female ACL means that females have smaller tendons for their size, indicating abnormal loading mechanisms. This is proven when assessing the strength of the ligaments between the two genders. Finding that male ligaments were able to have a higher force applied on them (20). First noted in animal models, the effects of an increasing concentration of estrogen have been shown to stimulate fibroblasts to produce matrix metalloproteinase, which in turn degrades collagen. The opposite effect has been shown with progesterone (21,24). Studies have even confirmed the presence of estrogen and progesterone receptors the human ACL (25) which has led to a variety of studies. One study performed was able to find a significant correlation between ACL injury in alpine skiers during the preovulatory phase of the menstrual cycle rather than postovulatory (23). It is important to note that an effect of hormones on ACL elasticity has been observed, with the highest elasticity during ovulation (26). Through this increased elasticity and as a result increased translation, the odds of sustaining an ACL injury were 4-fold. (27). Therefore, while a plethora of factors are involved there is a common consensus that a gender like predisposition exists.

### *Anatomy*

A predisposing factor as discussed is the female gender. However, the reasons why this is so have to be taken into account. There exist modifiable and non-modifiable factors when considering ACL injury (4). Modifiable, as the name indicates, are factors that can be adjusted, these can include prevention programs, training and athlete education. Non-modifiable are factors that cannot be altered such as genetic predisposition, anatomic variances, and hormonal levels. One such important factor is the intercondylar notch width ratio index (NWR), this is the

ratio between the distal femur width and the width at the level of the popliteal groove. A study by Tarek et al. was performed on 902 athletes at a high school level and found a significant difference in the NWR between males and females (6). Specifically that males, who suffered less injuries in the recorded group had a higher NWR. The importance of this relationship is further confirmed when comparing the bilateral, unilateral and lack of ACL tearing with respect to the opening notch width of the femur. It has been reported that patients who suffered bilateral ACL rupture did indeed have smaller notch opening width (7). Although notch width is a contributing factor to increasing the likelihood of rupture, it is not the only, as was shown in a study of military subjects which found BMI to have a significant correlation when comparing male subjects who suffered ACL and those who didn't. That was that a higher BMI ( $26.5 \pm 3.5$ ) was found in subjects who suffered rupture, while those who didn't had a mean BMI of  $24.7 \pm 2.9$  (10). However, there was no significant relation between BMI and rupture in female patients. A study that assessed the coronal aspects of the safe, provocative and hyper-provocative landing positions found that the tibial slope in the provoking positions is more towards 90 degrees than in the safe position (8). Thus we can conclude that tibias with greater slopes are at an anatomically greater risk, especially when this angle is amplified with abnormal landing positions, to lead to ACL rupture. The synergistic action of the slope with the anterior translation of the tibia during provoking movements leads to an even further increased risk. This concept of provoking movements has been further elaborated by Walden et al. when discussing mechanisms of ACL rupture in soccer players. Analysis of slow speed footage has revealed patterns in injury. Those are that high velocity, sudden cutting movements, or abnormal landing positions where the majority of the athlete's weight is translated onto the injured leg lead to an initial contact with the ground in a position of hip flexion and genu valgum, this results in rupture of the ligament

(9). The consistent observation of the knee in valgus position during the initial contact of the athlete with the ground is in line with further observations that greater force is generated when the tibia is in internal rotation while extended or flexed rather than external rotation (12). Another investigation found that in a group of high school level athletes, that athletes who suffered ACL injury had 8.4 degrees greater valgus at initial contact with the ground and 7.6 at maximal contact (14). Increased hip adduction can lead to increased loads on the knee, thereby resulting rupture (15). Abnormally high relative strain forces have been observed in females than in males (22). This is explained through Pauwels forces, the anatomic position of coxa vara leads to an adaptation of the body to develop weaker hip abductors due to the length of the fulcrum being closer to the weight exerted on the hip joint by the body. This neuromechanical theory of injury is further proven by analysis of how efficient are prevention programs that focus on neuromuscular strengthening. For example, when comparing a control group of athletes and a group following the FIFA 11+ warm-up program. We observe a significant reduction in ACL injury within the intervention group (16).

### *Age*

There seems to exist an inherent connection between age and ACL injury. As elaborated on, NWI is a factor predisposing to injury. This remains true even in the pediatric population finding that non-contact ACL rupture occurred in patients with smaller NWI (28). The trouble with such skeletally immature patients is whether to perform surgery or leave with conservative treatment. However, studies have shown that patients younger than twenty years have poorer morphological recovery than older patients (29). This has been theorized to be due to the more active nature of

younger individuals, leading to macroscopically worse ruptures thus resulting in poorer recovery. In regards to the previously discussed points on neuromuscular control, there is further discussion to have in order to highlight the relation of trunk lateralization and knee injury (30). Poor trunk control has been associated with an increased incidence in athletes, the same is to be said in pediatric populations. The importance of educational programs in youth should not be overlooked. During a study performed by Thompson-Kolesar et al., preadolescent athletes displayed greater initial contact and peak knee valgus angles during all activities when compared with the adolescent athletes (31). When subjected to prevention programs the preadolescent subjects improved and decreased their initial contact knee valgus angle. Therefore younger athletes, while having improper biomechanics which can lead to ACL injury, can adapt to improve their biomechanics. The result of these improper biomechanical techniques is believed to be why younger patients often suffer more serious injuries (29). As discovered by a twenty-one year population based study performed by Sanders et al. the average age of ACL rupture when accounting for both sexes was found to be 68.6 (32). Regarding the effects of menopause on female ACL's, no human studies have been done. However, animal models done on rabbits have shown no additional laxity in menopausal rabbits when compared to younger ones (33). The effects of estrogen levels on the human knee are clear (24, 34) but whether menopause has a direct link to increased incidence of ACL rupture remains unstudied. A study by Schilati et al. found the mean age of ACL tears to be 29.4+-11.7 (35). They also found that the incidence decreases with age, which is most likely due to the declining participation in sports at an advanced age. However, in a descriptive epidemiological study done, there has been an increase in ACL revisions in an outpatient setting from 43% in 1994 to 95% in 2006 (36). There are two reasons for this increase, the first has been cited to be due to an increased desire in older patients

to stay physically active. The second is the ever growing average life expectancy around the world, noting that a majority of this increase was due to younger patients under twenty and patients over forty. To further explore why younger age groups are contributing more to revision rates a study by Snaebjornsson et al., showed that an early age of receiving surgical intervention has also been linked to increased revision rates (37). Therefore through analyzing these studies we are able to prove that high level sports are being pushed on increasingly younger patients, which in turn lead to increased rates of rupture and therefore increased rates of revision. The adaptability of this younger population group, as previously mentioned is an important factor to consider. Knowing full well that increased numbers of primary surgeries and revisions, can lead to financial strain on the health care system.

## **Diagnosis**

In order to identify potential ACL tears it is important that we look at etiological causes. As previously mentioned gender, anatomy and age are key predisposing factors that must be taken into account when diagnosing ACL ruptures. Being aware to these predisposing factors we can then begin to evaluate a patient keeping in mind differential diagnoses. Usually the case presents as a sudden “pop” during a provocative movement or trauma, which can lead to swelling potential hemarthrosis. When a pediatric case is presented it is important to rule out tibial eminence fracture with radiographs, these fractures are more common during puberty (38,39). Patellar stability must be checked as patellar dislocations can mimic ACL tears. Lachman and pivot shift tests can be normal, even better results can be obtained when done under anesthesia, it is important to perform the clinical test under these conditions as it can yield higher specificity

(39). The KT-1000 can be used to evaluate knee laxity. The presentation in a skeletally mature patient is very similar, and therefore the diagnosis of such cases should follow the same format. Magnetic resonance imaging (MRI) should be used to confirm clinical diagnosis.

### **Past Techniques in ACL repair**

Due to poor imaging modalities and lack of clinical tests, ACL ruptures went unnoticed. Furthermore, the act of performing surgeries on cases with instability during the pre-antibiotic era was daunting and therefore of little concern. Tearing of the ACL was first described in its primitive form by Hippocrates, however, he was not able to accurately describe the ligaments involved. Rather saying that following a traumatic knee incident with subsequent instability, there has to be some involvement of ligaments (41). Further work was done since this by physicians the followed suite, elaborating the function of the ACL and observing the instability created when the ligament is cut, later described as the anterior drawer test. The following discoveries of the primitive form of the Lachman and pivot-shift tests were made, later to be popularized. It was not until William Battle that the first ever documented successful ACL repair was performed in 1900. A simple suturing of the distal and proximal components of the ACL was made with a good outcome. Although, there was debate as to how effective this technique was as there had to be ample ligament proximally to attach the distal part to, which in the majority of cases was not true. This led Georg Perthes to devise a method where he created a tunnel in the distal femoral head, just under the insertion of the ACL. Emerging around the same time was the technique developed by Erwin Payr. The technique used a semicircular tunnel and fascia lata loop running through the tunnel connecting the proximal ligament to distal. Eventually the futile efforts of suturing a completely ruptured tendon with poor remnants led to a school of



thought to completely replace the tendon. Hey Groves was one of the early pioneers of such replacement techniques, developing an approach that utilized the fascia lata. Removing the muscle from its tibial attachment site and running it through a canal drilled into the lateral side of the femur and through a tibial canal, suturing it onto the periosteum. This method was fast expanded on due to increased abduction of the knee and strain on the graft. Different approaches were developed, a medial para-patellar approach taken by Charles F Eikenbary was meant to spare the patella. ACL surgery was popularized in America very quickly leading to the Hey Groves method rapidly developing the bone block ilio-tibial band transfer method by Insall. The technique involved detaching the central portion of the fascia lata with its osseous insertion from Gerdy's tubercle, re-routed the graft over-the-top of the postero-lateral femoral condyle through the joint and secured the bone block with a screw. However Insall himself commented on the instability of the knee after using this method. The idea of allografts was thought to be a safer alternative to autografts as to not create instability elsewhere by harvesting from the patient. Although viral transmission was found to be a huge stumbling block, meanwhile radiation methods were found to disrupt the collagen structure of the grafts. Thanks to advancements made, today allografts are viewed as an alternative to autografts (43). Bruckner first mentioned using the medial third of the patellar tendon (PT) and bone (42), however, it was not mentioned in English literature until Franke revisited the idea. The patellar tendon bone graft quickly became a popular choice of graft. However, the complications of the surgery made a need for an alternative graft, today the choice is from the biceps femoris muscle. Single band reconstructions caused further instability in pivot-shift tests, therefore the theory of reconstructing both the anteromedial (AM) and posterolateral (PL) bands became of interest. This theory was eventually confirmed by Yasuda et al. when they reported better results whilst reconstructing both bundles.

The advent of the arthroscopic era, first popularized in 1970s, further contributed to ACL reconstruction. During the first few years, there were several limiting factors to ACL surgery, most notably the cumbersome nature of the instrumentation and the proximity of the surgeon's eye to the rod lens system led to serious concerns of deesterilization. However, as the technology progressed so did the benefits of arthroscopic surgery; decreased recovery time, improved range of motion (ROM), lessened post-operative morbidity. (44)

### **Present day ACL Repair Techniques**

#### *Type of Graft*

The first choice that should be considered when regarding ACL repair is the type of graft the patient should receive. The choice between allograft and autograft, according to a meta-analysis performed by Li-Kan et al. they found the autograft to be the superior choice with regards to strength and knee stability (43). When comparing BPTB autografts to allografts, a study performed by Kraeutler et al. concluded that, autografts should be used in younger patients due to the lower rupture rates and higher patient satisfaction (51). Using such a graft, the rate of failure is lower possibly due to the immune reactions that can occur with foreign grafts. The theory for these perceived higher failure rates of allografts is debated today, there exist several theories and the answer is likely an amalgamation of all existing concepts. Nevertheless, the allograft has therefore been used sparingly in younger populations and more in older patients as allografts have been shown to have outcomes similar to those of autografts in this population. The disadvantages of autografts are increased donor site morbidity, which is why the preference in these patients are allografts. Citing quicker recovery times and decreased donor site morbidity,

both of which are crucial when operating on elderly patients, as potential reasons why this graft is favoured to autografts (46). Another factor to consider in allografts is the costly irradiation step required, with less than 2.2 Mrad and lower temperatures (dry-ice) needed to lessen the rate of graft failure (45). The higher the radiation, the more potential it has to cause collagen damage ending in increased laxity post-operation. This is potential for increased laxity is why allografts have been favoured more as attempts to salvage what knee function in revision after initial graft failure. Although it has been observed that allografts result in increased joint laxity this has been theorized to be due to the ligamentization process that progresses more slowly than with autografts (46). After an allograft reconstruction is performed, the graft undergoes several process leading up to ligamentization, first the early acute inflammation, this inflammation leads to necrosis with no visible vascularization. The subsequent recruitment of cells results chronic inflammation and therefore vascularization which in turn leads to proliferation and collagen remodelling, thereby ending in ligamentization (47). Some authors have even suggested the use of allografts in younger patients who participate in sports that place greater relative loads and velocities on the knee (49). The disparity in choosing graft type lies in the technique of the surgical centre, allografts prove trickier with more variables to account for needing proper allograft screening, irradiation method and temperature. Further studies have shown successful outcomes when accounting for all of these factors (48). As a result the decision whether to use allograft or autograft should be made based by a combination of the patient's lifestyle, whether the patient is involved in strenuous sporting activities and their desire to return to full function. The patient's age, do they have a poor prognosis for healing of the autograft site? In other words does the increased donor site morbidity outweigh the potential benefits of ACL repair? Lastly,

the centre's experience in grafts, whether they have the resources to treat allografts with the required irradiation and storage or the proper screening procedures to minimize patient harm.

### *Graft Site*

However, depending on the habits of the patient, taking into account the activity level, the activities the patient is involved in and the age, we can more clearly visualize which graft is better suited. The lifestyle heavily influences the site from where the graft is harvested, the surgeon has several options to consider. Younger patients might be more involved in sporting activities such as basketball, soccer, football and handball. These are activities where lateral cutting and quick decelerations and accelerations create a need for stability and strength in the knee. The generally favoured graft type in these younger more active patients are autografts, as previously established. Once the type of graft is decided, the next parameter to take into account is whether to use a hamstring graft, BPTB or quadriceps. There are several disadvantages to the patellar tendon graft, one of them being quadriceps weakness with a relatively slow recovery (51), although authors have theorized this could be due to the rehabilitation regimen rather than graft type (53). Using the bone and tendon for a graft leaves the donor site with a defect. Some authors have reported rupture of the patellar tendon after its use to autografting the ACL (52). Others have reported patellar fracture, medial and lateral subluxation of the patella, although these are mostly limited to case reports (53). Reports done by histological analysis combined with Magnetic resonance imaging have shown cases where the tendon has resumed normal tendon structure (54). Furthermore, other published works have shown no patellofemoral complications post-operation with BPTB autografts. The BPTB while in theory creating a defect

causes very little complications, mostly anterior pain (56,57,58,59,61,62), and when combined with its strength and long term survival rates creates the optimal graft when considering a patient for such procedure. Noyes et al. have shown the strength of such grafts to be four times greater than native ACLs (55). This is useful when considering athletes who wish to return to a high level of physical activity as proven by Xie et al. who showed that athletes receiving BPTB autografts have an odds ratio for return to preinjury level of 1.48 (57). Therefore, this graft is ideal in professional athletes or those who wish to return to their preinjury level and should be avoided in patients in whom anterior knee pain would be debilitating for example: carpenters, painters, plumbers etc. (50). But of course the complications of the graft in vivo depends on a multitude of factors, fixation, extent of necrosis and also the remodelling process (58). While there are clear advantages and disadvantages to the BPTB graft. The high variety in post-operation complications leads us to hypothesize that, surgical skill level and experience with the type of graft is a large component in choosing the right graft. The ideal graft is one that: would involve the use of a graft that is easily harvested, results in little harvest-site morbidity, has biomechanical properties equal or superior to those of the native ligament, possesses high initial strength and stiffness, can be secured predictably with rapid incorporation, and allows early aggressive rehabilitation while recreating the anatomy and function of the native knee (61). The next graft to consider is the hamstring (HT) graft. This graft presents an alternative to BPTB grafts in one particular way, the significant reduction in anterior knee pain (57). The advantages of the HT graft as previously mentioned is the lack of anterior knee pain, however there is also higher preservation of the extensor mechanisms (57). In fact the quadruple stranded HT graft (4SHT) has been shown to have a tensile strength three times greater than that of the native ACL (58). The load failure of the grafts has also been noted to be higher than that of the BPTB graft,

2422N and 1784N respectively (60). It has been noted that at 2 year follow up comparing BPTB and 4SHT grafts there was no statistical significant among any outcome measure other than the 4SHT group able to walk earlier (63). A common complication of such graft harvesting in 39.7% to 88% of patients is the patellar incision which can cause damage to the infrapatellar branches of the saphenous nerve, leading to paresthesia. This complication can be diminished by using an oblique or horizontal incision (64,65). However, the long term effects are still debated, whether graft failure is more common in 4SHT or BPTB grafts with some studies finding no correlation (62). While there exists much debate whether the patellar tendon graft or the hamstring graft are superior, many forget about the quadriceps tendon (QT) as a potential graft site. One study found even 10 years after surgery. There was no pain at the donor graft site in the medium and long term. The rate of return to sport was excellent and there were no changes in the patellofemoral joint (66).

### **Potential Future Options**

Modern medicine has come a long way since the advent of ACL repair, minimalizing the mortality rate associated early with this operation. The inventions of different graft types and sites has made a variety of options that can be tailored to suit the patient's lifestyle. However, we must be wary of complacency and ideally put efforts towards eliminating complications as much as we can. While the BPTB and HT grafts have been long regarded as the two main grafting sites for ACL repair many have forgotten about the QT graft. The benefits of the QT graft were shown as early as 1999 (69). The quadriceps muscle has 20% more collagen fibrils per cross sectional area than the patellar tendon, meaning that its failure load is 70% greater than a similar width PT graft (67). Furthermore, newer studies show that there are no statistical differences between HT

and QT studies (68,70). While the size of the HT graft is mostly the right fit, the PT is often too small the QT is oversized (71). This oversizing issue can be supplemented by centralizing the graft harvest and only using a partial harvest (70). Some experienced complications of such a harvest can be damage to the perforating vessels causing post-operational bleeding and therefore compartment syndrome (70). However, this could be due to improper technique and it could be decreased by using a less aggressive harvesting technique. No current technique is perfect, this need for improvement is what lead us to renewed interest in synthetic grafts. Synthetic ligaments became popular in 1980 and the early 1990s. First generations were woven, braided or knitted, these early models were prone to breakage. Complications ensued such as sterile effusion due to carbon fibers and early rupture (72). Second generation were braided with longitudinal and transverse fibres which were woven out of Dacron and Polytetra Fluorethylene. This generation allowed for fibroblast incorporation but still suffered from wear and fraying. Third generation synthetics, such as the active biosynthetic composite (ABC) or the Ligament augmentation reconstruction system (LARS), have an extraarticular knitted portion and no braiding to reduce particle wear. However their use remains controversial (59). Rupture rates for both are still high, although LARS has proven to be less problematic (72). The Bridge enhanced anterior cruciate ligament repair (BEAR) has also been devised as a consequence to inadequate grafts. This synthetic graft is an extracellular matrix scaffold that is placed between the torn ends of the ACL to bridge the gap, healing is activated by the patient's blood. Initial human studies done by Murray et al. have shown the BEAR repair method results as comparable to those of 4SHT autograft over the first 24 months (73). However they concluded that further study is required.

## **Conclusion**

Anterior cruciate ligament rupture is a serious burden on the world's health care system. The medical community has worked hard on finding the predisposing factors to this injury. We now know that gender, anatomy and age can all play crucial roles in the etiology of the injury. Which is why the modifiable factors must be minimized in order to avoid surgical intervention. The methods for identifying and repairing these tears have dramatically improved throughout the last 50 years. The grafts and techniques have attributed to decreased mortality and improved quality of life post-injury. It is imperative that complacency is not the correct way moving towards the future. There exist alternatives to autografts and allografts that should be further pursued.



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