Research Progress in Pathogenesis and Treatment of the Anterior Cruciate Ligament Injury

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Abstract. With the continuous development of the sports in China, sports trauma is also on the rise year by year, of which the former cruciate ligament injury is quite common. Anterior cruciate ligament (ACL), one of the two main types of intraarticular fibrous ligament, it can provide the rotational and translational stability for the knee. When it injuries, patients' exercise ability and life well-being will decline, and even lead to a series of complications, especially in women. The risk of the ACL injury in the women is almost 3.5 times that in men. There are many factors leading to ACL injury. Studies have shown that after anterior cruciate ligament injury, most patients choose surgical treatment. With the development of the Arthroscopic technique, most of the patients would be likely to choose the surgical treatment, especially the people that are young and active. The surgical treatment have several advantages, like the post-operative recovery is fast, less traumatic, fewer complications. At present, the surgical treatment is mainly reconstruction under arthroscopy. The reconstruction materials include autografts, allografts, artificial ligaments and so on. It is necessary to understand the difference of biochemical and biological characteristics of different grafts in the process of ligament healing. For some elderly patients or patients with other special needs, non-surgical treatment can also be selected. This article reviews the pathogenic factors, surgical methods, grafts, and other aspects for clinical reference.

Keywords: Anterior cruciate ligament injury, pathogenesis, treatment

1. Introduction
Anterior cruciate ligament (ACL) is a key structure inside the knee joint connecting the femur and tibia, which is used to resist different types of loads, and if it is lacking, it can lead to instability of the anterior tibia and rotation. According to statistics, ACLI reaches 200000 people in the United States every year[1]. And the number is increasing year by year.

At present, with the change of people's lifestyle and residents' attention to sports, its incidence rate is still rising. This injury can have huge affect on some athletes. Most of them can no longer perform as well as they used to and some of them even have to stop their careers. And in the same situation, female athletes always have a higher risk of getting ACL injury than male athletes. The female athletes had 1.5 times the incidence proportion and a 1.7-fold increase in the incidence rate of ACL injury compared with males[2].

Many factors may lead to ACLI, like external and internal factors. At present, ACLI treatments are mainly divided into surgical treatment and non-surgical treatment. The surgical treatment have several advantages, like the post-operative recovery is fast, less traumatic, fewer complications. However,
surgery can only reconstruct the anatomical structure of patients, and there are still some deficiencies[3]. From the perspective of ACLI, this paper explores the anatomic structure, pathogenic factors, pathogenesis and treatment progress of ACLI, so as to provide help for the diagnosis and treatment of ACLI in the future.

2. Risk of the ACLI

2.1. Anatomical factors
ACL, one of the two main types of intraarticular fibrous ligament, it can provide the rotational and translational stability for the knee[4]. Some scholars think that the ACL is consisted with 3 parts, which is anteromedial, intermediate and posterolateral bundles[5]. While other authors divide the ACL into the 2 bundles, the anteromedial bundle(AMB) and posterolateral bundle(PLB). In fact, the two-bundle theory is widely accepted compared with the three-bundle description. From the functional perspective, the ACL is the primary stabilizer for the knees, which is responsible for preventing the anterior translation and also the rotation of the tibia on the femur. The length of ACL is about 22-41mm, and the width is about 7-12mm [5-7].

2.1.1. Q angle. Athletes that suffer or have suffered from the ACL injuries always have a quite larger Q angle than the athletes that do not have the ACL injure. Additionally, the Q angle of the male (the number is 51) and the female (the number is 51) had been measured by Herrington and Nester, the result shows that females have a larger Q angle than males, which can be an explanation of why females have a higher ACL injury risk. Gray J et al states that no apparent relationship between ACL injury and the Q angle[7]. Therefore, Q angle is a questioned factor and still need to be proved.

2.1.2. Intercondylar notch. Nowadays there are conflicting theories about the relationship between getting ACL injury and the intercondylar notch width(INW). And some researchers have showed that INW is smaller in females than males. Others stated that NWI itself is not a factor of the ACL injury and the shape of the notch effect the injury as well. Teitz et al compared the NWI of 40 men and 40 women and their result is that there is no different between male and female. The current research results are not unified.
According to Anderson et al, only 6% of the normal knees had a wave-shape notch. However, 35% of unilateral ACL injured patients had the wave-shape notch[8]. The reason why the result of different authors seems to be controversial is varying measurement techniques and the reliability of these techniques. In conclusion, it still needs further researches.

2.1.3. High posterior tibial inclination (PTS). PTS is also the risk factor. In knees with ACL loss, tibial anterior displacement increased by 6 mm when PTS increase 10°. A retrospective analysis shows that compared with the ACL-intact group, in the ACL-deficient group, the medial posterior tibial slope(MPTS) and lateral posterior tibial slope(LPTS) were significantly higher at 25%, 50%, and 75% (P = .00001). Similarly, they have sex difference (P = .00001) [9].
Systematic review included 20 studies confirmed that increasing of the PTS was related to the increased the risk of the ACL transplant failure after reconstruction[10]. The increase of PTSA is sometimes associated with the ACL degradation.

2.2. Hormonal factors
One of the reason that why females are at higher ACL injury risk is that hormones act differently between sexes. Many studies on the effects of hormones of the ACL have focused on the level of the circulating hormone within the menstrual cycle, such as estrogen and or relaxing. If estrogen is reduced in the body, the production of collagen is reduced, which may lead to the decline of ACL strength. Some studies believe that the vasoilation effect of estrogen can increase tissue water content and destroy the stability of ligament. Relaxing reduces the tensile strength of ligaments by releasing

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metalloproteinases that cause collagen to break down[11]. However, whether there is a direct relationship between the hormonal factors and the ACL injury is still controversial and the research and discussing about this one is still going on.

2.3. Neuromuscular factors
Muscle reaction time and the time to peak torque can be understood for an examples of the neuromuscular control, which reflect the speed of the knee joint reaches stability. And it will clearly affect the possibility of getting ACL injury. Measurement of muscle strength may be crucial in preventing injuries in male or female youth athletes. Especially in female athletes, a decrease in hamstring strength was a risk factor for injury compared to matched healthy men.

In addition, if the EMG muscle pre activity of the lateral hamstring muscle is reduced relative to the lateral EMG of the quadriceps femoris, the risk of the ACL injury in the elite female handball and the football players may be higher[12].

2.4. Extrinsic factors
In most cases, extrinsic factor refers to environmental factor. The environmental factor includes the equipment, the temperature and so on. For example, the footwear, especially those can provide greater torsional protection seems to be associated with higher ACL injury.

Among male professional players, previous studies have found that coaching style can affect team injury, and frequent coaching changes can also lead to increased muscle injuries. Among female professional players, 20.8 percent of ACL injuries occurred during a coaching change during the season[13].

3. The treatment of ACLI

3.1. Surgical treatment
With the development of the Arthroscopic technique, most of the patients would be likely to choose the surgical treatment, especially the people that are young and active. The surgical treatment have several advantages, like the post-operative recovery is fast, less traumatic, fewer complications[14]. The most prevailed operative method of the ACL injury is the Arthroscopic reconstructive surgery. It is one of the reconstruction method. The American Academy of Orthopedic Surgeons’ 2016 guidelines for the ACL injuries management suggest arthroscopic reconstructive surgery for the vast majority of patients with ACL injuries[15].

What reconstruction means is that using grafts to reconstruct a new ligament. And the timing of the surgery, the range of motion before surgery, the swelling and the strength of the quadriceps can be seen as the important factors which may affect whether the reconstruction will finally succeed. The Arthroscopic reconstruction can divide into to detailed methods, which is the single-bundle reconstruction (SB) and the double-bundle (DB) reconstruction. SB reconstruction refers to the commonly used reconstruction method to limit the tibial relative to the femur. It has the advantages of the low operation difficulty, the short operation time and the small revision difficulty, but it also has some certain limitations, such as the poor effect in rotation function. DB reconstruction can not only restore the the knee joint anterior straight stability, moreover, the rotational stability and natural anatomical structure of the knee can were restored [16].

Some studies have compared the effects of the SB and the DB techniques in different ways. The results show that the DB technique can obtain better knee stability, but the postoperative function is similar to the SB technique. However, some studies got the opposite result. It is not clear which technique is more effective in terms of clinical outcomes [17].

3.2. Graft
Although the reconstructed ACL can not completely be restored to the original anatomical structure of the ACL, the grafts that are used for the reconstruction must have the characteristics and
characteristics very similar to the original ligament, and also have the minimum antigenicity and sufficient biological characteristics. Potential for integration into host bone[18].

3.2.1. Autograft. Autograft refers to replacing the native ligament with a new one taken from the patient himself, which includes fascia late, iliotibial fasciculus, popliteal tendon (gracilis and semitendinosus), bone patellar tendon bone (BPTB), quadriceps femoris tendon, etc[19].

Although the tensile strength of iliotibial band as ACL graft is close to normal ACL, some study have confirmed that the tensile strength is slightly lower than that of BPTB, and the tendon and bone healing is slower than that of BPTB[20].

A retrospective analysis that involved 112 patients, and they were divided into 2 groups, allogeneic tendons group (n=58) and autologous hamstring tendons group (n=54). It probed that the reconstructed ACL with allografts were similar to the autographs. There was no significant difference, especially the postoperative infection and the disease transmission[21].

3.2.2. Allograft. At present, the allogeneic tendons commonly used in ACL reconstruction include BPTB, tibialis anterior or posterior tendons, Achilles tendons, peroneus longus tendons, etc. Allogeneic BPTB and tibialis anterior or posterior tendons are the most widely used. However, there is no consensus on the ideal allograft type. In the field of allograft, Guo L et al states that Irradiated, chemically processed, or preserved allografts are often chosen over fresh-frozen allografts, which produce results comparable to autografts[22].

3.2.3. Artificial grafts. In the 1980s, artificial grafts became to be used for the ACL reconstruction. The graft of non-absorbable polyethylene terephthalate is called LARS. This is a third-generation synthetic ligament designed to create the network that can repair the joints, also prevent reactive synovitis problems[23].

3.3. Non-surgical treatment
Non-surgical treatment mainly includes the physical therapy, the anti-inflammatory and analgesic drugs, the range of motion training, and the strength training of quadriceps femoris and calf muscles. It is sometimes suitable for some patients, particularly for the old. While there are some disadvantages of the non-surgical treatment, such as higher likelihood of getting osteoarthritis (OA) and higher possibility of suffering meniscal injuries[24]. How to choose surgical and non-surgical treatment depends on clinical conditions and patient needs.

4. Conclusion
Anterior cruciate ligament (ACL), one of the two main types of intraarticular fibrous ligament, it can provide the rotational and translational stability for the knee. The ACL injury is a common orthopaedic disease, which affects mostly women. Aslo, the incidence rate of young children is gradually increasing. Seriously affect people's quality of life, which needs our attention and early diagnosis and intervention in clinic. However, even if they are diagnosed early, treated surgically and rehabilitated early, the anterior cruciate ligament of most patients will not recover to the previous functional level and will develop into knee arthritis and osteoarthritis.

The factors related to anterior cruciate ligament injury include abnormal anatomical structure (Q angle, Intercondylar Notch, PTS), changes in hormone levels (explain why there are gender differences in the disease), neuromuscular defects and biomechanical abnormalities, as well as external factors such as environment and site.

Most of the patients would be likely to choose the surgical treatment, especially the people that are young and active, because it has several advantages, like the post-operative recovery is fast, less traumatic, fewer complications. Reconstruction is one of the commonly used surgical methods. At present, there is no final conclusion about the effect comparison between double beam reconstruction and single beam reconstruction. There are many options for the reconstructed graft. It is crucial to
understand the difference of biochemical and biological characteristics of different grafts, especially autografts and allografts (because these two kinds of grafts are most widely used in clinical practice) in the process of ligament healing.

At present, there is no accurate theoretical basis for clinical and basic research on this issue, the high-risk factors need further discussion lack of large sample size research. A large amount of evidence-based evidence is still needed to support it in the future.

References


