Advance of Treatment of Anterior Cruciate Ligament (ACL) Injuries of the Knee

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Abstract: This paper offers a comprehensive overview of anterior cruciate ligament (ACL) injury in sports involving dynamic movement in terms of epidemiology, diagnostic workup, therapeutic management, and rehabilitation innovation. ACL injury in such sports is classified into partial tears, complete ruptures, and combined injury, with 70–80% caused by non-contact mechanisms due to biomechanical imbalances. Diagnosis is presented in terms of various modalities, namely physical examination (e.g., Lachman test), MRI (gold standard for imaging soft tissue), ultrasound, and X-rays, with a description of their hierarchical use: primary screening through physical examination and X-rays, and MRI confirmation in the majority of instances, with ultrasound for dynamic follow-up in select groups. Treatment is differentiated between surgical (autografts, allografts, artificial ligaments) and conservative (rehabilitation, bracing, new biologics), with surgical reconstruction for active patients and conservative management for elderly or comorbid patients. Rehabilitation protocol outlines phased steps with the use of neuromuscular training, proprioceptive exercises, and new technology in the form of photobiomodulation (PBM) for reducing inflammation and aligning collagen, and surface electromyography (sEMG) feedback for optimal pattern of activation of the muscles. Innovation in the article lies in its tiered diagnostic streamlining, enabling context-specific combinations of imaging modalities (e.g., MRI-ultrasound synergy in pediatric injury), as well as in its focus on new rehabilitation technology for functional optimization. By spanning various disciplines of knowledge, the study delineates the path towards individualized medicine as well as better outcomes for ACL injury, bridging lacunae in early detection, minimally invasive procedures, and individual rehabilitation templates.

1 INTRODUCTION

Originating from the posteromedial aspect of the lateral femoral condyle, the anterior cruciate ligament attaches onto the anterior intercondylar portion of the tibia, just anterior and slightly lateral to the medial intercondylar tubercle, and partially blends with the anterior portion of the lateral meniscus. Its collagen bundles are separated into anteromedial and posterolateral bundles, and it inserts anterior to the tibial intercondylar eminence (Standring, 2021). The ACL physiologically preserves the mechanical stability of the knee during dynamic movement by restricting anterior tibial translation and regulating rotational and internal and external rotational forces. The tension in the anteromedial (AM) bundle escalates with knee flexion, while the posterolateral (PL) bundle has heightened tension during extension and in reaction to linked internal rotation (Georgoulis, A D et al., 2010).

Based on the degree of ligament injury and associated structural involvement, ACL injuries can be divided into three primary categories: partial tears, total ruptures, and combined injuries. A partial loss of knee stability results from partial tears, which are caused by partial ligament fiber rupture that preserves continuity. Complete ruptures indicate complete loss of continuity of the ligament, resulting in significant instability of the knee joint. Combined injuries are commonly linked with meniscus injury, medial collateral ligament or posterior cruciate ligament damage, and articular cartilage damage. These types have a direct impact on the choice of clinical treatment strategy and prognostic assessment.

As one of the most common musculoskeletal conditions, ACL injuries' frequency has increased rapidly in the past few decades. Between 200,000 and 250,000 ACL injuries occur annually in the United States. About 25% of these injuries occur in children under the age of 18, and men are more inclined than

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women to suffer a ruptured ACL overall, mostly as a result of playing in more team and contact sports (Arundale, Amelia J H et al., 2022). But when it comes to physical activity, women are regularly proven to be more vulnerable, even though men sustain most injuries since they are more likely to engage in athletic activities (Gianotti, Simon M., et al., 2009). Sex differences in anatomy, hormones, neuromuscular control, and kinematics are most likely the reason of the discrepancy in ACL injury rates. Males and females differ in the neurological regulation and biomechanics of the hips and trunk in each of the three planes of motion (sagittal, coronal, and transverse). Females exhibit more lateral trunk displacement, higher trunk and hip flexion angles, and wider trunk motion ranges than males. Due to differences in landing techniques between the sexes, as well as their increased joint laxity and decreased torsional stiffness, females may be more prone to ACL injuries (Hewett, Timothy E et al., 2016). Across all youth sports, female athletes have an almost one in ten thousand chances of suffering an ACL injury, which is nearly 1.5 times the risk for men athletes; a female athlete who participates in several sports is thought to have a roughly 10% chance of suffering an ACL damage during her time in high school or middle school. Adolescents who play soccer, basketball, lacrosse, and other sports, both male and female, are especially vulnerable to injury (Bram, J. T., Magee, L. C., Mehta, N. N., Patel, N. M., & Ganley, T. J., 2021).

Anterior cruciate ligament (ACL) injuries are usually triggered by abnormal loads placed on the knee, and the specific mechanisms can be categorized into two types: contact and non-contact injuries. Non-contact injuries account for 70%-80% of ACL injuries and are not caused by direct external impacts, but by uncontrolled movement of the knee joint itself during sports. Non-contact injuries are most common in sports that require rapid changes of direction, jumps or sharp stops. For example, when a soccer player stops sharply to turn, the knee is in a position of flexion, valgus (inward buckling of the knee), and external rotation, at which point the shear forces of anterior tibial translation and rotation can exceed the tolerance limits of the ACL, resulting in ligament tearing. A similar situation occurs when a basketball player lands unsteadily on one foot after a jump, or when a skier changes direction during a sudden deceleration in a high-speed glide. In a specific case, during a basketball game, a 23-year-old man had a non-contact pivoting injury to his left knee while changing direction and slowing down. He was unable to support his weight after feeling a "pop" in his knee. As soon as the court helped him, he realized that his knee was swollen. Although pain and swelling limited examination during the acute phase, the collateral ligaments were found to be clinically intact. A full, mid-substance ACL rupture was seen on a magnetic resonance imaging scan (Wall, Chris et al., 2023). 95% of ACL injuries sustained by Norwegian top division handball teams during two seasons happened without any player contact, according to a registry that documents these injuries (Dai, B., Herman, D., Liu, H., Garrett, W. E., & Yu, B., 2012). The common feature of these maneuvers is that the knee joint is subjected to abnormal stresses due to biomechanical imbalances during dynamic motion. The core causes of non-contact injuries are related to several biomechanical factors. The first is knee valgus (internal buckling); when landing with the knee at an internal buckling angle of more than 8 degrees, the load on the ACL spikes to more than three times its normal value. The second is muscle coordination imbalances, particularly quadriceps overpowering and hamstrings delaying activation to effectively limit anterior tibial translation. In addition, inadequate strength in the core muscles can lead to a shift in the center of gravity of the body, further exacerbating torsional stress on the knee joint. Foot problems such as flat feet or excessive internal rotation can also alter force transmission pathways and increase the risk of ACL injuries. Conversely, contact injuries occur when the knee is directly subjected to external forces. The ACL is subjected to tensile or shear stresses that exceed its physiological limits as a result of contact with the outside knee, which causes excessive anterior tibial translation, external rotation, or internal rotation. Higher energy mechanisms of injury are usually the cause of contact-type mechanisms. Traumatic knee dislocations or high-energy on-field injuries may fall under this category. Similar to the non-contact injury, hyperextension, or collision, can occur when the knee experiences valgus or varus stress in the form of translation and shearing motion (Wetters, Nathan, et al., 2016). This finally leads to a ligament rupture. Typical scenarios for this type of injury include a sideways scoop in soccer, a tackle against a tackle in rugby, or a direct hit to the knee in a traffic accident. For example, in rugby, when an athlete's knee is hit laterally by an opponent at a high speed, the knee momentarily externally rotates and combines with rotation, which often leads to a combined injury of the ACL and the medial collateral ligament (MCL), or even accompanied by a meniscus tear. Another risk factor is due to sex and hormones.

2 DIAGNOSIS

Symptoms and signs of anterior cruciate ligament injury change dynamically at different stages. In the acute stage of the injury, patients often feel sudden and severe pain during knee flexion movements (such as stopping sharply, jumping, and landing). They typically report a popping sound followed by sudden knee pain and swelling, using the "double fist sign"—that is, rotating their fists in a grinding motion with their faces facing each other—to express their sense of instability (Cimino, Francesca, Bradford Scott Volk, and Don Setter, 2010). Within 1-2 hours after the injury, intra-articular hemorrhage due to ligament tearing leads to the rapid formation of obvious hematoma, at this time, the joint is swollen and bulging, the skin temperature rises, the activities are severely limited, and the flexion and extension movements can cause sharp pain. In the following 24 hours, the fluid accumulation gradually increased, causing persistent swelling and pain. Patients complain of knee “tenderness” or “misalignment” when walking, especially when turning around or walking up and down stairs, and some are forced to adopt a “bent-knee gait” due to acute pain and quadriceps muscle inhibition (inability to contract the muscles on their own) that prevents them from completing straight-leg raises. Some people are unable to perform straight leg raises due to acute pain and quadriceps muscle inhibition (inability to contract the muscles on their own), and are forced to adopt a “bent-knee gait”—walking with the knee slightly flexed and the stride shortened to reduce the load. If not treated in time and enter the chronic stage, knee joint instability persists, repeated “giving way” phenomenon may occur in daily activities (such as walking, turning), and even sudden loss of control kneeling. Long-term instability leads to repeated small injuries to the joint, which can lead to secondary lesions: meniscus tear manifests itself as interlocking (sudden jamming during activities) and localized pressure and pain, while cartilage abrasion manifests itself as persistent hidden pain, morning stiffness or swelling after activities. Physical examination reveals atrophy of the quadriceps muscle (due to long-term pain-avoidance muscle inhibition), a further decrease in joint mobility (less than 90° of flexion and limited extension), and early signs of osteoarthritis (e.g., friction sensation in the joints) in some patients. According to prior research, even though ACL restoration is common, as many as 80% of patients may experience knee osteoarthritis (OA) in the ten to fifteen years afterwards (Azus, Aisia, et al., 2018).

Physical Examination examines the functional integrity of the ACL by reproducing the force status of the knee joint through biomechanical maneuvers, for which three methods are regularly used. Firstly, the Lachman test: the patient lies supine, the examiner keeps the distal femur clamped with one hand and moves the proximal tibia anteriorly with the other hand (20°-30° knee flexion). Its positive form is an increase in anterior tibial displacement with no end point, 85%-90% sensitive, most reliable test in the acute phase. Second, the anterior drawer test: the tibia is drawn anteriorly with the knee flexed to 90° in order to assess anterior laxity. As the hamstrings are able to contract compensatorily in the flexed position, the sensitivity is reduced to 60%-70% and is more applicable to chronic injuries. Thirdly, axial shift test: passive extension of the knee and valgus stress, progressive flexion of the knee when the tibial epicondyle "misalignment sensation", high specificity (>90%), but requires the patient to relax, difficult to cooperate with the acute phase due to pain. The Physical Examination benefits are non-invasive, immediate patient feedback, and low cost. However, its disadvantages are that the findings are operator-dependent, false negatives may occur in the acute phase due to swelling or muscle spasm, and the degree of injury cannot be quantified. Therefore, Physical Examination is suitable for acute initial screening and sports-side assessment.

Magnetic Resonance Imaging (MRI), a high-resolution soft tissue imaging technique, can directly view the ACL's continuity, the tear's location, and any associated lesions (such as meniscus and cartilage damage). Additionally, it possesses high safety, multiparameter, and multiplanar imaging features. For ACL damage, MRI direct signs—that is, direct pathological alterations at the lesion site—had a high diagnostic value. Of these, ACL edema and thickness, discontinuity, and abnormal alignment have a significant diagnostic value (Zhang, Y. J., Jiang, Y. Y., & Liu, C. H., 2024). MRI has very high soft tissue resolution, with a diagnostic accuracy of greater than 95%, and can differentiate between a partial tear (partial fiber continuity) and a complete break. It is appropriate for pregnant women and children and does not emit radiation. It is important to note, though, that MRIs are often 10–20 times more costly than X-rays. Additionally, it is time-consuming and could result in false-negative findings for minor injuries or chronic scarring.

Ultrasound utilizes high-frequency sound waves to dynamically scan the ACL and is suitable for visualizing the ligament morphology and status in motion. The normal ACL is diagnosed ultrasonographically as a homogeneous, highly echogenic fascicle extending from the lateral femoral condyle to the intercondylar ridge of the tibia. Injury to the ACL manifests itself as localized hypoechoicity (edema), interruption of fibers, or thickening (scarring). The benefits of ultrasound include being radiation-free, portable, and suitable for screening children, pregnant women, and low-resource areas. Its real-time dynamic evaluation capacity allows for the observation of changes in ligament tension during knee flexion and extension. However, ultrasound necessitates a high degree of technical expertise from the operator, who must be familiar with the knee's anatomy. And, deep structures, such as the posterior bundle of the ACL, have inadequate resolution. Imaging quality is reduced in obese or severely swollen patients. Therefore, ultrasound is often used as a complement to MRI rather than as a stand-alone diagnostic tool.

Computerized Tomography (CT) is used to accurately visualize bony structural abnormalities (e.g., complex fractures, intercondylar ridge avulsions) through three-dimensional bone imaging, and is used for polytrauma or preoperative planning. CT has good diagnostic value for knee fractures because it can visualize the bony structure of the knee, with the advantage of rapid scanning and clear bone detail. However, due to the high water content of ligamentous tissue, the relatively uniform density of soft tissue, and the lack of significant density changes after injury, CT findings do not allow for a definitive assessment of the severity of ligamentous or soft tissue injuries. At the same time, CT carries a risk of radiation exposure, so it is usually used only when there is a suspicion of combined severe fractures. Since it is less likely to produce a comprehensive image and direct visualization of the ACL, CT can only be utilized in conjunction with indications of fracture, osteoporosis, tibial dislocation, and bone contusion (Sun Yadong & Zhu Limin., 2023).

Diagnostic X-rays show bony structures through penetrating X-ray imaging, commonly used positions include orthostatic, lateral, and intercondylar fossa (tunnel view). The direct signs are usually not abnormal, but it is possible to rule out a tibial plateau fracture or an ACL stop avulsion, which is an avulsion of the intercondylar ridge. The indirect sign of a Second fracture (avulsion fracture of the lateral tibial plateau) is highly suggestive of an ACL injury (specificity >90%). X-rays have the advantages of being efficient (completed in less than 5 minutes), economical, and widely available. It suggests the possibility of ACL injury through indirect signs. However, X-rays do not directly show ligament or soft tissue damage and are of limited diagnostic value for simple ACL injuries. They are only used as an adjunctive tool to initially rule out skeletal problems. Therefore, X-rays are suitable for acute trauma to rule out fractures and for preoperative skeletal morphology assessment.

3 TREATMENTS OF ACL INJURIES

The aim of ACL treatments is straightforward. Its goals are to address deficits, restore functional stability, and safely return to sports; to be specific, there are several phases: the acute phase after the injury focuses on the elimination of residual symptoms (effusion and pain) and impairments (range of motion and quadriceps activation), the subsequent phase includes neuromuscular and perturbation training to improve knee stabilization, and the final phase aims to further optimize muscular strength, return to preinjury sport level through specific exercises, and assess psychological readiness for the return to sport (Diermeier, Theresa Anita, et al., 2021). The decision on different types of treatment is essential as well. Factors that affect the decision may include patients' age, physical activity level, types of injuries, etc. There are two main types of treatments: Surgical Treatment and Non-Surgical Treatment (Conservative Treatment).

3.1 Surgical Treatment

The main surgical approaches include replacing the ACL with a patellar tendon autograft, popliteal tendon autograft, quadriceps tendon autograft, or a tendon graft consisting of a patellar tendon, Achilles tendon, or popliteal tendon allograft. This treatment is primarily indicated for younger patients with a complete ACL rupture who require a return to sport or have a combined meniscal reparable injury or other ligamentous injury. Currently, the main common surgical approaches include autograft, allograft, and artificial ligament reconstruction. Surgical Treatment has a long-term success rate of 82% to 95%.

The most common surgical treatment is an autograft. Specifically, patellar tendon-bone grafts can help provide excellent initial stiffness and fixation strength in athletes who require a high degree of knee stability. However, this treatment may lead to donor area complications such as anterior knee pain or patellar tendinitis, resulting in compromised postoperative rehabilitation.

Another common autograft technique is hamstring tendon grafting using the thin femoral and semitendinosus muscles. Although it is slightly weaker compared to patellar tendon-bone grafts, it can reduce patient pain and donor site complication symptoms. It is crucial to remember that in the postoperative phase, the popliteal tendon may become lax, which can negatively affect the long-term stability of the knee.

Allografts are an alternative option in surgical cases faced with multiple ligament injuries or requiring revision surgery. However, the use of allogeneic grafts carries a potential risk of immune rejection and infection, so they must be thoroughly examined and managed.

Artificial ligaments such as LARS (Ligament Advanced Reinforcement System) are very useful for patients who wish to recover quickly during specific surgical procedures. Unfortunately, its use is limited by its high wear rate and risk of re-rupture.

In terms of surgical technique, minimally invasive ACL reconstruction using arthroscopic assistance significantly reduces postoperative pain and tissue damage and speeds up recovery compared to traditional open surgery. There are two types of reconstruction: anatomic single-bundle reconstruction and double-bundle reconstruction. Double-bundle reconstruction is anatomically closer to the distribution of the original ACL and theoretically provides better rotational stability. However, it is technically complex and time-consuming, so it is not applicable to all patients.

The post-operative rehabilitation phase is also a key part of treatment. It requires following a scientific, staged rehabilitation process. The main considerations include joint mobility, muscle function, neuromuscular control, modifications related to the type of graft, meniscal repair, and ligamentous co-surgery. Postoperative rehabilitation is usually divided into three phases: 0 to 6 weeks to protect the graft, limit activity, and prevent re-injury; 6 to 12 weeks to restore knee mobility and plyometrics, with a gradual return to weight-bearing; and 3 to 6 months to the reconstruction of athletic function in preparation for return to athletic activity or competition. The whole rehabilitation process should be carried out under professional guidance to ensure the stability of ligament reconstruction and complete recovery of knee function.

3.2 Non-Surgical Treatment (Conservative Treatment)

Although surgery is the preferred treatment for most people who experience an ACL injury, conservative treatment is also an effective option. It is mainly for patients with fair stability of the partially torn cut knee, especially the elderly and non-athlete population. It is also recommended to prioritize non-surgical treatment for patients with contraindications to surgery such as severe cardiopulmonary disease.

The core of conservative treatment is systematic rehabilitation, which is usually carried out in stages. In the early treatment phase, the focus is on controlling joint swelling and pain, using the “POLICE” principle (Protection, Optimal Loading, Ice, Compression, Elevation), and starting passive and active Range of Motion (ROM) training to prevent joint stiffness. At the same time, passive and active ROM training is started to prevent joint stiffness. In the middle stage, the focus of rehabilitation shifts to neuromuscular control and strength training, especially hamstring and core muscle strengthening training, which helps to enhance the stability of the back of the knee; at the same time, proprioceptive training needs to be carried out to improve the patient's perception of the position of the knee joint and the state of the movement, to prevent accidental sprains. In the late stage, functional training is the main focus, simulating daily activities or mild sports movements, laying the foundation for the recovery of life functions or even some sports functions.

In addition, the knee brace occupies a significant role in conservative treatment. It prevents anterior shifting of the tibia and safeguards stability, reducing the risk of knee instability during sports. Recently, biological therapies such as platelet-rich plasma and stem cell injections are also gaining attention. Their goal is to promote ligament tissue regeneration by activating the body's local repair response. However, these therapies remain controversial in the management of ACL injuries and their effectiveness has yet to be proven.

Advantages of conservative treatment include avoidance of surgical risks, minimal trauma, flexible recovery cycles, and a paid-off financial burden. However, its limitations are also obvious. In demanding sports, it is challenging to reestablish a knee joint's dynamic stability, and may even increase the risk of secondary knee injuries in the long term. Therefore, when deciding whether or not to adopt non-surgical treatment, a detailed and careful assessment is required before making a decision.

4 REHABILITATIONS

4.1 The Standard in Traditional Physical Rehabilitation

The rehabilitation process after an ACL injury is also important as it enables knee function to return and the chances of re-injury to be reduced. The most widely employed standardized approach by physical therapists is generally separated into three phases, early, mid, and late, according to time post-treatment, to enable a progressive return of function.

The primary objectives for the first stage of rehabilitation (0 to 6 weeks after surgery) include the management of post-op reactionary swelling and pain, restoration of knee mobility, and early initiation of neuromuscular activation training. Compression and cold packs are the standard in swelling control, whereas using Continuous Passive Motion (CPM) machines is instrumental in restoring joint mobility and preventing adhesions. Simple exercises like ankle pump exercise and quadriceps isometric contractions are suitable for neuromuscular activation, prevention of muscle atrophy, and the basis for subsequent training.

The middle phase of rehabilitation (6 to 12 weeks after surgery) is aimed at the weight-bearing reconstruction and dynamic stability rehabilitation exercise. Closed-chain exercises, such as wall static squats, are considered less stressful to the joint with weight-bearing exercise and appropriate to aid with restoration of stability. Yet, open-chain movement (i.e., leg extension and flexion) can more effectively strengthen the quadriceps directly. The patients need to choose between the two exercises depending on their individual status and postoperative course. Dynamic balance training, however, enhances proprioception and coordination through the use of equipment like balance cushions. Improvement in dynamic balance was significantly and negatively related to the risk of re-injury in a study, and thus this phase of training is required (Grindem H, Snyder-Mackler L, Moksnes H, et al., 2016).

The key goal of the postoperative rehabilitation phase (12 weeks or more postoperatively) is to restore sport-specific abilities, particularly biomechanical control during jumping and landing. By evaluating and correcting the patient's knee forces and landing position during high speed sports, the Physical Therapist can effectively minimize the risk of secondary injury to the non-contact ACL. Only when biomechanical control is corrected can the knee have adequate functional symmetry and safety during high intensity sports.

4.2 Evidence-Based Breakthroughs in Emerging Rehabilitation Technologies

Rehabilitation approaches regarding ACL injuries continue to evolve and improve as rehabilitation therapy and technology converge. More and more emerging technologies are being introduced into clinical medicine and continue to be supported by research.

Photobiomodulation (PBM) is a non-invasive treatment. It induces biological levels at the cellular level by means of red light of a specific wavelength. In the early postoperative period after ACL surgery, the application of red light with a wavelength of 650 nm can significantly inhibit the release of inflammatory factors, thus reducing the local inflammatory response after surgery. Meanwhile, 810 nm near-infrared laser can promote the longitudinal alignment of collagen fibers. During ligament regeneration, this facilitates the reconstruction of tissue structure and the recovery of mechanical properties. This therapy, while still advancing, already has preliminary evidence to support its potential.

In the rehabilitation of ACL injuries, feedback from surface electromyography (sEMG) can help assess and train synergistic contractions of the quadriceps and hamstrings. sEMG monitors muscle activation in real time and helps patients correct their force generation style through timely feedback, thus improving knee stability. Failure of quadriceps activation as measured by EMG techniques remains a significant factor preventing full strength recovery after ACL reconstruction (Grooms, Dustin, Gregory Appelbaum, and James Onate, 2015). This finding supports the introduction of EMG feedback in postoperative rehabilitation to optimize training outcomes.

5 CONCLUSION

As a common and highly prevalent soft tissue injury in sports medicine, anterior cruciate ligament (ACL) injury of the knee has a profound impact on the patient's sports function and quality of life. Starting from the epidemiologic background of ACL, this article sequentially discusses its diagnostic methods, treatment means and rehabilitation strategies, and strives to provide systematic reference for clinical practice.

Currently, although imaging techniques such as MRI have found wide usage in the diagnosis of ACL, still there are limitations regarding early detection and precision. For treatment as well, both conservative and surgery have their positives, although the latter requires a program on case-by-case basis based on the patient's individual condition. Concurrently, ACL rehabilitation becomes necessary in a bid to reclaim knee function, and novel approaches such as optical therapy and neuromuscular training are gaining prominence as technology advances.

Combining the functions, advantages, and disadvantages of the ACL assessment methods mentioned above, the author summarizes the optimization and tiered application of the diagnostic process. Firstly, the initial assessment is based on Physical Examination combined with X-ray examination, aiming at the rapid exclusion of fractures and skeletal abnormalities. Secondly, MRI was preferred for confirming the diagnosis due to its high soft tissue fraction and multiplanar imaging capability, which can be used to clarify the extent of ligament and soft tissue injuries. Ultrasound, on the other hand, is used for dynamic monitoring and screening in specialized scenarios, such as resource-limited areas. In children, it is recommended that ultrasound screening be prioritized, thereby reducing radiation exposure, and then combined with MRI to confirm subtle injuries. In pregnant women and women of childbearing age, X-rays and CT Scans need to be strictly avoided, with MRI as the diagnostic tool of choice.

Overall, the diagnosis and treatment of ACL injury has gradually formed a more mature system, but there is still a broad space for development in terms of accurate diagnosis, minimally invasive surgery, and individualized rehabilitation. Future research should further integrate multidisciplinary means to provide patients with more scientific and efficient comprehensive treatment programs.

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