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# Management of Anterior Cruciate Ligament Rupture: A Narrative Review of Emerging Therapeutic Methods

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**ABSTRACT**

**Background.** Anterior cruciate ligament (ACL) rupture is a common orthopedic injury that significantly impacts athletic performance and long-term joint stability. While surgical reconstruction (ACLR) remains the current gold standard, there are concerns regarding graft failure, persistent rotational laxity, and the development of post-traumatic osteoarthritis.

**Aim.** This narrative review aims to analyze emerging therapeutic methods in ACL management, including modern surgical techniques, orthobiologic therapies, and tissue engineering, in terms of their clinical efficacy and limitations regarding their implementation to clinical practice.

**Methodology.** A literature search was conducted using PubMed, Web of Science, and Google Scholar. Meta-analyses, randomized controlled trials, and systematic reviews focusing on innovative therapeutic methods for ACL injuries were included.

**Results.** Primary repair with internal bracing and bridge-enhanced ACL repair technique show promise in joint preservation but are strictly dependent on tear morphology. Extra-articular augmentation have potential to reduce rotational laxity in high-risk cohorts. Platelet-rich plasma and mesenchymal stem cells may promote "ligamentization," though clinical evidence remains inconsistent due to a lack of standardized preparation protocols. Tissue engineering techniques, such as 3D bioprinting and electrospinning offer biomimetic potential, although there are significant regulatory and economic barriers.

**Conclusions.** Emerging therapeutic methods in ACL injury management offer promising advantages when combined with traditional ACLR. However, their widespread implementation

is currently limited by high costs, a lack of long-term clinical data, and the need for standardized application protocols. Future research is needed to determine their the long-term effectiveness of these techniques and and to define their precise role in routine clinical practice.

**Keywords:** Anterior Cruciate Ligament; ACL Reconstruction; Tissue Regenerarion; Bridge-Enhanced ACL Repair; ACL injury; Orthobiologics

## INTRODUCTION

Anterior cruciate ligament (ACL) rupture is one of the most common orthopaedic injuries, accounting for approximately 20% of all sport-related injuries of the knee joint. (1) It typically affects young and physically active patients, and usually occurs during physical activities that involve pivoting, jumping, or rapid deceleration, such as football, basketball, and skiing. (2–5) Structurally, the ACL consists of two bundles - anteromedial and posterolateral - which together play a crucial role in stabilizing the knee joint, particularly by limiting excessive forward movement of the tibia and providing resistance to rotational forces. (1–3,5) Rupture of the ACL results in immediate functional instability and compromised athletic performance. It has also been associated with long-term complications such as cartilage damage, meniscus injuries, and an increased risk of osteoarthritis, often leading to premature joint degeneration. (2–4,6,7)

For decades, the "gold standard" for managing these injuries has been surgical ACL reconstruction (ACLR) using autografts or allografts. (5,7) Although this approach has largely proven effective in terms of maintaining knee stability, it comes with several limitations. Firstly, ACLR often fails to restore normal joint kinetics, and may lead to persistent translational and rotational laxity. A significant number of patients treated with ACLR do not return to their pre-injury level of sport, and a substantial number of patients experience graft re-rupture. Secondly, evidence states that ACLR does not significantly reduce the risk of post-traumatic osteoarthritis, suggesting that current methods do not fully prevent biological degeneration of the knee joint. Additionally, the use of autografts is associated with tissue morbidity, while allografts carry the risk of biological integration failure and pathogen transmission. (8–12)

These challenges have started an ongoing debate regarding the optimal first-line treatment - early surgery versus primary rehabilitation. (1–3,5,6,13,14) Operative treatment remains the method of choice in young patients and those wishing to return to high-demanding sports. (15,16) However, the emerging evidence suggests that conservative treatment is also effective in certain individuals and may bring similar patient-reported functional outcomes compared to

surgical intervention. Consequently, the orthopedic community is currently facing a period of uncertainty where neither surgical treatment nor conservative approach can guarantee a return to pre-injury levels of joint integrity for all patients. In response to these challenges, recent clinical guidelines and consensus statements increasingly recommend an individualized decision-making approach. Multiple factors are taken into account when choosing the optimal therapeutic strategy, including the patient's level of physical activity, extent of injury, functional instability, and expectations regarding return to sport. (3,4,7,17)

This also prompted the development of multiple emerging techniques, including innovative surgical solutions aimed at preserving native ACL tissue, or advancements in biological and regenerative medicine to enhance healing of the ligament. (18–20) Moreover, novel strategies for adjunctive stabilization and personalized rehabilitation protocols have been introduced. (21,22) This narrative review aims to analyze the most prominent emerging therapeutic methods in the management of ACL rupture. These will include recent advancements in the following: ACL repair and augmentation techniques, biological and regenerative strategies, adjunctive extra-articular stabilization, and personalized rehabilitation methods.

## METHODOLOGY

This report is structured as a narrative review. The literature search was conducted across PubMed, Web of Science, and Google Scholar using the following keywords: "anterior cruciate ligament", "anterior cruciate ligament AND internal bracing", "bridge-enhanced ACL repair", "anterior cruciate ligament AND extra-articular augmentation", "orthobiologics", "anterior cruciate ligament AND platelet-rich plasma", "anterior cruciate ligament AND stem cells", "anterior cruciate ligament AND scaffolding", "anterior cruciate ligament AND bioprinting", "anterior cruciate ligament AND electrospinning".

The search included meta-analyses, systematic reviews, and randomized controlled trials that examined the emerging treatment approaches in patients with ACL rupture. Exclusion criteria eliminated case reports, studies of low methodological quality, and non-English publications.

## REVIEW

### 1. Emerging Surgical Innovations

#### 1.1 The Resurgence of Primary Repair and Internal Bracing

The surgical management of ACL ruptures is currently undergoing significant developments with a particular spike in interest concerning joint-preserving techniques. Historically, ACL

repair techniques involving direct suturing of the torn ligament ends were considered the best treatment method and the standard of care as far back as the 1970s and through the 1980s. (19) This approach, however, was largely abandoned due to unacceptably high clinical failure rates observed in follow-up examinations. The primary biological etiology of these failures was the hostile intra-articular environment of the knee joint due to the constant presence of synovial fluid, which contains high levels of the enzyme plasmin responsible for the premature dissolving of the fibrin clot biologically required to bridge the tear gap and initiate natural ligamentous healing. (23) The consequence of these experiences was a gradual shift towards complete tissue resection and mechanical replacement via autograft or allograft reconstruction. (20)

In recent years, modern primary repair has seen a renewed interest, driven largely by a deeper understanding of ligament healing and a more precise selection criteria. (19,20,24) Rather than applying primary repair universally, contemporary orthopedic surgeons rely heavily on the Sherman classification of ACL tears to identify suitable candidates. (19,20) The Sherman classification categorises ACL injuries based on the anatomical location of the rupture and the residual quality of the ligamentous tissue. (8,19)
Current clinical consensus dictates that the primary repair is strictly indicated for Sherman type I tears, proximal avulsions directly at the femoral footprint, or type II tears, provided the remaining ligament exhibits sufficient structural integrity capable of holding tensioned sutures. (5)

To overcome the biomechanical weakness that plagued historical suturing techniques, modern primary repair can now be augmented with a procedure known as internal bracing. This biomechanical concept involves placing a synthetic, ultra-high-molecular-weight polyethylene braided suture tape parallel to the repaired native ligament. The tape is firmly anchored into both the femur and tibia, effectively acting as an internal stabilization for the knee joint. (25–27)

The critical function of this suture tape augmentation is to stress-shield the healing ACL during the vulnerable early phases of healing, by absorbing peak physiological loads and restricting pathological anterior tibial translation during the vulnerable early phases of healing. The internal brace allows patients to undergo early postoperative mobilization and physical therapy without the risk of mechanically stretching or elongating the fragile, repairing tissue. (28–30)

### 1.2 Bridge-Enhanced ACL Repair (BEAR)

Building upon the biological principles of primary repair, the Bridge-Enhanced ACL Repair (BEAR) technique represents a great leap forward, moving the boundaries of mechanical repair towards tissue engineering. The mechanism of action for the BEAR procedure addresses the fundamental biological flaw of intra-articular ligament healing. The procedure utilizes a proprietary, bioresorbable bovine extracellular matrix (ECM) scaffold sponge that is surgically implanted between the torn ends of the ACL. (31–33) During the surgical intervention, the patient's own autologous whole blood is drawn and injected directly into the highly porous ECM sponge. The scaffold effectively acts as a protective housing, holding the resulting blood clot securely in place against the mechanically and chemically hostile synovial environment. By shielding the clot from plasmin-induced degradation, the BEAR scaffold supports cellular migration and regeneration of the native ligament tissue. (32–35)

The clinical evidence supporting the BEAR technique has been extensively studied. Notably, the BEAR II clinical trial provided landmark data comparing the outcomes of patients treated with the BEAR implant against a control group undergoing traditional autograft ACL reconstruction. At the two-year postoperative mark, the findings demonstrated that the BEAR procedure was statistically non-inferior to standard ACL reconstruction regarding anteroposterior knee laxity measured in objective arthrometric testing, as well as in patient-reported subjective functional outcomes and return-to-sport metrics. (34,36)

The advantages of the BEAR technique over traditional reconstruction align with the goal of minimum interference and joint preservation. Key among them is the preservation og the native tibial and femoral insertion sites. Maintaining these anatomical regions allows for the retention of vital proprioceptive mechanoreceptors and nerve fibers, which are irreversibly severed during graft reconstruction, preserving the patient's innate neuromuscular joint awareness. (37–40) Another advantage is the elimination of the necessity of autograft harvesting. This effectively eliminates all donor-site morbidities associated with ACL surgery, such as chronic knee pain from patellar tendon harvests or enduring flexor weakness from hamstring tendon harvests. (41–43)

### 1.3 Extra-Articular Augmentation

While primary repair and regenerative techniques address the intra-articular aspect of ACL injuries, emerging surgical innovations have also heavily focused on controlling the extra-articular biomechanics. In 2013, a landmark anatomical dissection study provided a clear qualitative and quantitative description of the anterolateral ligament (ALL), confirming it as a

distinct ligamentous capsule. (44,45) The ALL originates near the lateral epicondyle of the femur and inserts on the proximal tibia, positioned optimally to act as a secondary stabilizer against internal tibial rotation. (44)

The reason for targeting the anterolateral complex stems from the limitations of intra-articular ACL reconstruction. Biomechanical and clinical studies have demonstrated that standard, single-bundle ACL reconstruction alone often underdelivers in stabilizing the knee joint in rotating movements. This residual rotational laxity presents clinically as a persistent "pivot shift" phenomenon, which is correlated with poor subjective knee function, premature cartilage wear, and, eventually, could lead to graft failure. (46–48)

In response, surgeons have experimented with additional extra-articular augmentation techniques, specifically lateral extra-articular tenodesis and formal ALL reconstruction. These procedures are performed concurrently with ACL surgery to mechanically tether the lateral compartment, significantly reducing rotational laxity and offloading rotational forces from the haling intra-articular graft or repair site. (49–51)

It is important to note, however, that extra-articular augmentation is not universally indicated for all ACL ruptures. Major clinical studies, such as the STABILITY study, have established precise criteria identifying target populations who stand to benefit most from lateral extra-articular tenodesis or ALL reconstruction. These high-risk cohorts include patients exhibiting generalized benign joint hypermobility (such as those with elevated Beighton scores), patients undergoing complex revision ACL surgeries due to failure of a previous graft, and particularly young athletes (under 25), who intend to return to dynamic, high-pivoting sports where the rotational demands placed upon the knee are extreme. (52–57)

## 2. Orthobiologics and Regenerative Medicine

Orthobiologics are a broad range of biological substances used to modulate the inflammatory environment at the injury site and facilitate the healing process. These techniques include, among many, growth factors, stem cells, peripheral blood products, bone marrow-derived products, hyaluronic acid, gene therapy, or synthetic biomaterials. (18,58) In this narrative review, we specifically delve into platelet-rich plasma (PRP) and mesenchymal stem cells (MSCs), which have been selected due to their significant regenerative potential to revolutionize ACL rupture management.

### 2.1 Platelet-Rich Plasma

PRP is a concentrated suspension of autologous platelets in a small volume of plasma. It is obtained by centrifuging whole blood, which separates its components, allowing for the isolation of a platelet-rich layer. (18) The therapeutic potential of PRP is primarily attributed to the variety of growth factors released upon platelet activation. These include fibroblast growth factor (FGF), transforming growth factor beta (TGF-β), insulin-like growth factor (IGF), platelet-derived growth factor (PDGF), and vascular endothelial growth factor (VEGF). These factors are involved in promoting cell differentiation, angiogenesis, tenocyte and fibroblast recruitment, and the synthesis of ECM, thus collectively promoting tissue regeneration. (18,58,59) In the context of ACLR, it is hypothesized that PRP may promote tendon-bone healing by inducing vascularization and structural remodeling of the graft - a process known as "ligamentization". (60,61)

Current research has yielded inconclusive results regarding the efficacy of PRP in ACL injury management. Several meta-analyses and systematic reviews have demonstrated that PRP supplementation enhances early subjective functional scores, with most of the studies describing an improvement approximately 6 months after ACLR. (62–64) A systematic review and meta-analysis by Gan et al. found that the PRP group exhibited significantly higher International Knee Documentation Committee (IKDC) scores at 3, 6, and 12 months postoperatively compared to control groups. Additionally, Lysholm scores improved significantly 3 months after surgery. (62) These findings are partially supported by Zhang et al., who observed statistically significant improvements in subjective outcomes, as measured by IKDC and Lysholm scores, 6 months following ACLR. However, these improvements did not consistently reach clinically significant thresholds. Moreover, by the 12-month follow-up, any perceived functional advantage had diminished further. (61) On the other hand, a meta-analysis by Gang et al. found no improvements in IKDC or Lysholm scores following PRP treatment at any follow-up interval. (65) These findings suggest that the long-term functional impact of PRP in ACL injury remains uncertain.

Regarding pain management, multiple studies report that PRP administration significantly diminishes early postoperative pain levels. However, it does not provide long-term pain reduction. (59,61,62,65)

The impact of PRP on objective knee stability remains the primary point of debate. While a meta-analysis by Serag et al. reports that PRP may bring a significant improvement in postoperative knee stability, as supported by moderate evidence, other studies provide less optimistic conclusions. Zhang et al. reported that objective knee stability showed no statistically significant difference between the PRP and control groups. Furthermore, a meta-analysis by Zhu et al. concluded that while PRP facilitates earlier functional recovery, it does not significantly alter long-term knee function or improve overall graft rupture rates. (59,61,66)

The influence of PRP has also been analyzed in terms of the "ligamentization" of the graft, which is a critical phase of recovery. The results of recent randomized controlled trials by Gong et al. and Munde et al. suggest that intra-articular PRP supplementation may enhance early graft maturity. However, Gong et al. concluded that PRP had no significant effect on reducing bone tunnel widening or accelerating tendon–bone healing. Moreover, a meta-analysis by Zhang et al. reported that there was no statistical difference in tunnel enlargement after PRP administration compared to control groups. Consequently, the current evidence suggests that while PRP may improve graft maturation, its ability to prevent structural complications like tunnel widening remains unsupported. (61,67,68)

The main challenge regarding the widespread use of PRP is the lack of standardization, specifically regarding leukocyte levels and how many injections are needed. (64,69) Until standardized protocols are implemented, PRP should be considered an elective adjunct focused on early-phase recovery in ACL injury patients. (61,62)

### 2.2 Mesenchymal Stem Cells

MSCs have been extensively studied in recent years for their potential as a supportive treatment in ACL injuries. Recent evidence suggests that they may accelerate tendon-bone healing by enhancing cell proliferation and differentiation, therefore contributing to the formation of fibrocartilage and bone. The primary mechanism of action of MSCs involves the secretion of extracellular vesicles, specifically exosomes, which carry bioactive proteins, lipids, and nucleic acids to target cells at the injury site. Emerging research claims that MSCs-derived exosomes promote angiogenesis and osteogenesis, therefore improving graft reconstruction after ACLR. Moreover, MSCs exhibit endocrine and immunomodulatory properties, aiding the damaged tissues to undergo self-repair. They may secrete anti-inflammatory cytokines and polarize macrophages from a pro-inflammatory (M1 macrophage) to a pro-healing (M2 macrophage)

state. This modulation is crucial as it protects the graft from proteolytic degradation and enhances new bone formation around the tunnel. (60,70,71)

Preclinical studies on animals suggest that MSCs may enhance the structural integrity of the graft-tunnel interface. Histological examinations demonstrate that groups treated with MSCs exhibited significantly higher bone volume fractions compared to control groups. Specifically, greater cellularity, increased collagen deposition, and enhanced vascularization within the graft were observed in the MSCs groups. (72,73)

While preclinical data show promising results, their translation to clinical practice remains a challenge. Although an exploratory study by Moon et al. confirmed the safety of MSCs administration during ACLR, their authors questioned the functional superiority of MSCs use. In this study, the patients receiving human umbilical cord blood-derived MSCs showed no significant difference in objective knee stability or subjective functional scores at a 24-month follow-up when compared to standard ACLR groups. (74,75) However, promising results have been obtained in clinical trials regarding a combined therapy of MSCs + PRP. For instance, a randomized, double-blinded study by Lin et al. demonstrated that the intra-operative application of bone marrow aspiration concentrate in combination with PRP significantly improved objective knee stability. Specifically, a reduction in side-to-side laxity was observed. However, the subjective functional scores, including IKDC and Lysholm scale, did not significantly differ from the control group in the short-term follow-up period. (76)

This highlights the need to optimize protocols for MSCs to ensure that the observed biological enhancements in graft quality and joint stability translate into beneficial long-term clinical outcomes. (60,74)

**3. Tissue Engineering and Biomaterials**

The primary challenge in the move towards less invasive scaffold-based biological regeneration could be described as a sort of paradox. On one hand, the material used must be strong enough to withstand immediate postoperative mobilization while being porous and bioactive enough to allow for cellular infiltration and deposition of the ECM in the healing tissue, as well as tissue remodeling. (77–79)

### 3.1 Material types: Natural vs. Synthetic

In the hierarchy of biomaterials, scientists categorize scaffolds into natural and synthetic polymers, each presenting distinct trade-offs in degradation and strength. Natural polymers, specifically Type I collagen and Silk Fibroin, are frequently cited for their excellent biocompatibility. Collagen, as the primary structural protein of the native ACL, provides intrinsic advantages such as easier cell attachment. However, high-quality studies indicate that pure collagen scaffolds lack the mechanical durability required for proper stabilisation of the knee joint, frequently exhibiting enzymatic degradation that outpaces the rate of new tissue formation. Silk Fibroin has emerged as a robust natural alternative as it is characterised by superior tensile strength and a slower, more predictable degradation rate. (80–82)

Conversely, synthetic polymers like polycaprolactone (PCL) and polylactic acid offer high-fidelity control over mechanical properties. PCL is favored for its slow degradation (often over 24 months), which provides a stable scaffold for long-term healing. However, synthetics are inherently hydrophobic, which can lead to poor cell seeding efficiency and potential for “stress shielding” - a situation where the scaffold carries too much load, preventing the developing tissue from strengthening. Current trends in medical literature point toward composite scaffolds - using a PCL core for strength and a collagen coating for its bioactive potential as the most effective strategy for balancing these competing needs. (83–86)

### 3.2 Electrospinning: Mimicking Native Structure

The native ACL is a highly organised tissue characterised by anisotropic alignment, meaning its collagen fibers are oriented in a specific direction to resist the tensile forces of knee rotation and translation. Electrospinning is the premier manufacturing technique to replicate this structure. By applying a high voltage charge to a polymer solution, ultrafine nanofibrers are ejected toward a collector. When combined with a high-speed rotational force in the collector, the fibers are deposited in a parallel, longitudinal orientation rather than a mat of randomly interwoven fibers. Research confirms that this directional alignment is vital for “contact guidance”. When Mesenchymal Stem Cells or ACL fibroblasts are seeded onto these aligned fibers, they physically elongate and align themselves along the fiber axis. (87,88) This alignment triggers the expression of scleraxis and tenomodulin, essential for ligament-specific differentiation. Without this directional topography, cells tend to adopt a disorganised, myofibroblastic phenotype, leading to a decrease in strength to linear forces during exercise. (87,89)

### 3.3 Bioprinting and the Tri-phasic Interface

While electrospinning excels at creating the mid-substance of the ligament, it struggles to replicate the complex enthesis (the connection between the bone and the ligament). This is where 3D bioprinting can lead to a revolution in this area. The concept is based on creating patient-specific constructs by translating MRI and CT DICOM data into a blueprint. This allows for the fabrication of a graft that fits the patient's unique femoral and tibial tunnel dimensions, reducing the risk of graft mismatch, which is a leading cause of early ACL revision surgeries. (90–92)

The most significant advancement in this sector is the development of Tri-phasic Constructs. In nature, the ACL does not insert into the bone abruptly; the connection transitions through four distinct zones: ligament, non-mineralised fibrocartilage, mineralised fibrocartilage, and finally bone. Recreating this connection is exceedingly difficult, but it has the potential to limit the chances of stress shielding and graft pull-out. Bioprinting enables a gradient approach, depositing different cell-laden materials in a sequential matter, with the goal of mimicking the natural structure. (93,94)

Clinical research suggests that these bioprinted gradients could significantly improve the distribution of mechanical strain. (95,96) In traditional ACL reconstruction using autografts, the connection is the weakest link; bioprinted scaffolds allow for a biological 'interlocking' where the bone grows into the scaffolds while the middle becomes a flexible, fibrous cord. Furthermore, the use of materials such as Pluroolic F-127 during the process allows for the creation of micro-channels within the scaffolds, which facilitates angiogenesis, addressing the problem of core necrosis in thick tissue-engineered constructs. (97–100) By integrating MRI-based precision with multi-material gradient printing, bioprinting offers a pathway toward a 'living' ACL replacement that can remodel and grow with the patient, a feat that is impossible with synthetic and highly limited with autografts. (101,102)

## 4. Challenges and Future Directions

Despite substantial progress in the development of novel strategies for managing ACL injuries, they are inevitably linked with certain limitations. Firstly, extensive safety and efficacy data is required for each of these methodss in order for them to be approved and implemented into widespread clinical practice. Secondly, the costs of development and widespread implementation of these techniques are high. As a result, access to these innovations may

initially be limited to specialized centers, elite athletes, or patients with greater financial resources. (103) Finally, the field faces a significant challenge related to the standardization of biologic therapies, particularly PRP and MSCs treatments. Current clinical studies use widely varying preparation techniques, platelet concentrations, and injection protocols, making it difficult to compare results across trials. (104) Establishing standardized preparation methods and reporting guidelines will be essential for generating high-quality evidence and determining the true clinical value of these therapies.

## CONCLUSIONS

Emerging surgical, biomechanical and regenerative strategies show promising potential as adjuncts to standard treatment in ACL rupture management. However, their clinical application remains limited by variability in protocols, high costs, and a lack of long-term evidence. Further high-quality, standardized studies are required to determine their effectiveness and optimal use of these methods in day-to-day practice.

## DISCLOSURES

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