Partial Anterior Cruciate Ligament Lesions: A Biological Approach to Repair

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52.1 Introduction

The anterior cruciate ligament (ACL) is a critical stabilizer of the knee joint, helping to control rotational tibiofemoral motion, and motion in the anteroposterior plane. ACL injuries are an often cited cause of functional limitation with respect to a wide range of activities, from recreational to elite sporting competition. Anterior cruciate ligament reconstruction (ACLR) is the current gold standard treatment for ACL insufficiency, with high success rates for return-to-play typically reported [1, 2]. There are notable disadvantages of ACLR that include increased complication rates in adolescents, loss of proprioception, donor side morbidity, incomplete return to high-demand sports, and the inability to restore normal kinematics of the knee joint [3–5]. Considering that ACL injury most commonly affects a younger demographic, leading to substantial morbidity and lifestyle modification, therapeutic options that are capable of restoring near-anatomic function of this ligament have the potential to overcome a number of the disadvantages associated with current ACLR techniques. The optimal treatment of partial ACL tears is a subject of considerable debate in the field of sports traumatology. Techniques of arthroscopically assisted ACLR have been used successfully to treat all types of ACL injury. In the event of partial ACL rupture, surgical management may include standard ACLR techniques that are used to treat complete rupture, or a more directed approach may be employed. Surgical repair of the disrupted liga-

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ment, or selective reconstruction of the injured ACL bundle, may be considered in the case of partial ACL rupture. Theoretically, preserving the native ACL will minimize loss of proprioception and avoid morbidity associated with autologous graft harvesting [6]. Advances in the understanding of cellular repair mechanisms and the increasing availability of various biologics may factor prominently in future treatment algorithms for certain types of ACL injury.

52.2 Basic Science and Classification

A variety of experimental models have been used to examine the anatomy of the ACL, as well as the physiologic reparative responses to injury [7–10]. Degeneration of the ACL has been observed following acute rupture, and this is associated with a significant increase in collagenase activity within the articular space [7]. The healing potential of the ACL is known to be poor, and markedly inferior to the healing capabilities of other ligaments such as the medial collateral ligament (MCL) [8]. Experimental data from in vitro studies has demonstrated that the outgrowth of cells from ACL tissue is slower compared to that of MCL tissue [8, 11]. These findings suggest an inferior capacity for cellular proliferation and migration in cases of ACL injury. Furthermore, animal experiments have identified increased procollagen mRNA in the MCL in comparison to the ACL, which suggests a reduced capacity for collagen synthesis and subsequent tissue repair after injury to the ACL [10]. Fibrin clot formation is an important component of ligamentous repair, and this process has been shown to be impaired in cases of ACL disruption. Plasmin within the joint space is capable of inhibiting fibrin clot formation [12]. Without this clot, disrupted fibers of the ACL remain detached, which reduces cellular migration and limits the potential for healing. Additionally, synovial fluid has been shown to impair the proliferation of ACL fibroblasts, thereby further reducing the capacity for spontaneous tissue healing [13].

Currently, there is inconsistency in the literature with respect to the classification of partial ACL lesions (Fig. 52.1), and significant variability in clinical practice with regard to preferred treatment methods. In work published by Noyes et al., these injuries were categorized according to the region of the tear, degree of ligamentous injury, and the relationship of ligament bundles to the tibia [14]. Gobbi et al. classified partial tears of the ACL into four categories, based on MRI findings of bundle disruption that were confirmed under arthroscopic examination by probing (Table 52.1) [15].

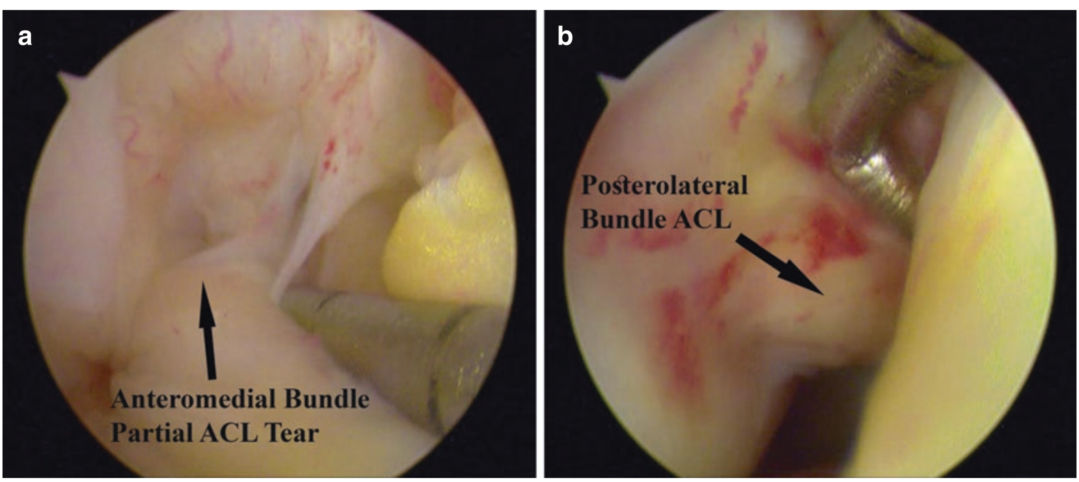

Fig. 52.1 Partial anterior cruciate ligament tear demonstrating disruption of the anteromedial bundle (**a**), with an intact and edematous posterolateral bundle (**b**)

Table 52.1 Gobbi classification of anterior cruciate ligament injury

Type I	Partial lesion (<100%) of anteromedial bundle, posterolateral bundle intact
Type II	Partial lesion (<100%) of posterolateral bundle, anteromedial bundle intact
Type III	Anteromedial and posteromedial bundles partially torn (<100%)
Type IV	Complete ACL tear of both anteromedial and posterolateral bundles

52.3 Primary Repair of the Anterior Cruciate Ligament

The natural history and poor healing potential of ACL injury has been described in the literature. In a prospective study, Noyes et al. estimated that 50% of patients with partial tears affecting more than half of the ACL would progress to complete ACL insufficiency after conservative treatment [14]. Additionally, a study by Braggion et al. reported that some patients undergoing arthroscopy during the acute stage of ACL injury were classified as suffering an incomplete ACL lesion, whereas arthroscopy performed during the chronic stage of injury revealed a complete tear in all cases [16]. Sommerlath et al. reported a mean Lysholm score of 93 points in 22 patients after acute partial ACL tear [17]. Nineteen of these ACL injuries were treated conservatively, while three underwent surgical repair of the torn ligamentous fibers. In contrast to Sommerlath et al., Buckley et al. reported that only 44% of 25 patients were able to resume sports after conservative treatment of arthroscopically documented partial ACL tears [18]. Fujimoto et al. evaluated conservative treatment and spontaneous healing of partial ACL tears in low demand patients [19]. In his study, 74% of patients had a stable knee at 16 months post-injury.

Although the first ACL repair has been described as early as 1895, primary suture repair of the torn portions of the ACL was popularized five decades ago [20, 21]. Feagin et al. reported a technique of ACL repair after acute injury using a polyglycolic acid suture woven through the tibial stump and passed up through bone tunnels in the femur [22]. Long-term follow-up studies demonstrated that this technique led to failure rates up to 90% and was therefore abandoned in favor of ACL reconstruction [14, 22, 23]. Despite these reports, recent investigations have demonstrated the potential of ACL healing after primary suture repair of the ligament augmented with the use of growth factors and bone marrow-derived mesenchymal stem cells (MSCs) [24–28].

52.4 The Role of Growth Factors and Platelet-Rich Plasma (PRP) in ACL Repair

Tissue healing is dependent on a number of bioactive substances that coordinate processes of healing such as cellular differentiation, proliferation, migration, and the deposition of supportive extracellular matrices. These factors can be found in abundance within platelet-rich plasma (PRP) and have been shown to enhance many stages of tissue repair [29]. In the clinical setting, PRP is typically used to stimulate the natural healing cascade and to augment tissue regeneration by providing a concentrated release of platelet-derived factors directly at the site of injury. Platelet-rich plasma is isolated after centrifugation of autologous venous blood, usually extracted and processed using a commercially available system. Importantly, it has been shown that there is significant variability in PRP growth factor constituents, depending on the method used for separation. Among the growth factors contained in PRP, platelet-derived growth factor (PDGF), fibroblast growth factor (FGF), bone morphogenetic protein (BMP), and transforming growth factor beta (TGF-β) are notable constituents that have been shown to enhance ligamentous healing.

The effects of plasma rich in growth factors on return-to-play in a series of patients suffering from partial tearing of the ACL was examined by Seijas et al. [30]. The majority of these active patients returned to pre-injury activity levels after treatment, and follow-up MRI imaging typically demonstrated complete restoration of ligamentous integrity after 1 year. In a study by Kobayashi et al., improved vascularity and ligament healing of injured canine ACL was demonstrated following application of basic fibroblast growth factor (bFGF) [31]. Targeted application of bioactive factors in other animal models such as transforming growth factor beta 1 (TGF-β1), growth differentiation factor 5 (GDF5), and bone morphogenetic protein 2 (BMP2) have demonstrated enhanced collagen synthesis and healing response in treatment of ligamentous injury [32–34]. Other research, however, has failed to demonstrate enhanced ACL repair in animal models using PRP augmentation [6].

52.5 The Role of Mesenchymal Stem Cells in ACL Repair

Mesenchymal stem cells are multipotent cells that reside in a variety of tissues including bone marrow, muscle, synovium, and adipose tissue. These precursor cells have self-renewing capabilities and are able to differentiate into a number of tissue types, making them an attractive target for cellular therapy in a range of clinical applications [35, 36]. There is potential for these cells to be used in reparative treatments for ACL injury due to their shared characteristics with ligament outgrowth cells [24, 37]. There are specific deficiencies of cellular repair that impact healing of injured ACL tissue, and MSC therapies have the capacity to influence reparative processes at the cellular and molecular level. One of the earliest methods used to augment healing processes after ACL injury was described by Steadman and involved microfracture within the intercondylar notch to release elements containing MSCs and growth factors contained within the marrow, which had the proposed effect of aiding clot formation and augmenting cellular repair processes [25, 38].

Our center has analyzed 5-year clinical outcomes after primary suture repair of partial ACL tears in addition to microfracture about the ligament footprint within the intercondylar notch, followed by application of PRP to the repair site [15]. Of the treated cohort, 78% returned to sporting activities, and there was a significant decrease in the side-to-side difference in anterior tibial translation at final follow-up. Based on this data, it was concluded that this technique could be used effectively to restore knee stability and enable return-to-sport in young patients treated for acute partial ACL tear. Currently, our preferred method of biologic augmentation in cases of partial ACL repair involves application of bone marrow aspirate concentrate to the repair site (Fig. 52.2).

There have been other reported series that have examined the use of intra-articular injection of bone marrow aspirate concentrate to treat ACL injury that have demonstrated improvement in ligamentous integrity according to MRI criteria at follow-up assessment [39]. Biologic augmentation of reparative and reconstructive methods to treat ACL injury will continue to evolve, and work will continue to determine the ideal constituents of PRP and MSC preparations that will optimize tissue healing [9].

52.6 Future Developments

Techniques that involve biologic augmentation of ACL repair in cases of partial ACL injury, and their role in restoring knee stability, will continue to progress. The potential for these agents to act synergistically in biologic cascades of cellular repair is encouraging; however, clinical application of these factors needs further study. As knowledge of cellular and molecular biology progresses and technological advances in tissue engineering proceed, composites of cell-scaffold materials will likely lead to greater advancements in therapeutic approaches to restore near-normal anatomy in cases of ligamentous injury. In cases of ACL injury, such composite treatments would be capable of providing structural support and an environment partially sequestered from circulating plasmin, while also providing growth factors and precursor cells to enhance reparative processes.

Conclusions

In the case of symptomatic partial ACL injury in the active patient who wishes to return to demanding physical activities that require restoration of knee stability, surgical treatment is often preferable early in the course of management, as there may be progressive symptomatic laxity and increasing dysfunction. While selective reconstruction of the injured ACL bundle may be performed, standard ACL reconstruction technique may also be used to restore stability, and comparative analysis of selective bundle reconstruction and standard reconstruc-

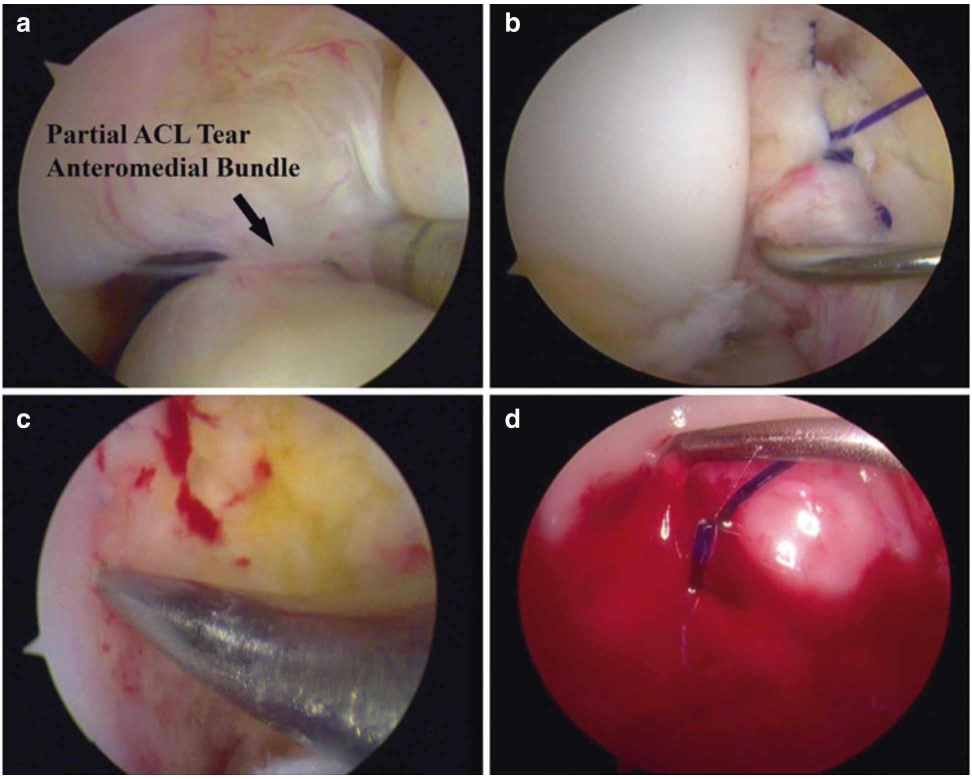

Fig. 52.2 Partial anterior cruciate ligament (ACL) tear involving the anteromedial bundle (**a**). Arthroscopic suture repair of the ACL using no. 1 PDS suture (**b**). Marrow stimulation about the ACL footprint within the intercondylar notch using a microfracture awl (**c**). Application of activated bone marrow aspirate concentrate to the repaired partial ACL tear (**d**)

tion for these cases of partial ligamentous injury is lacking. The technique of ACL repair with biologic augmentation in select cases of partial ACL injury that has been performed at our institution has demonstrated comparable results to those that would be expected with standard reconstructive methods. Further outcome analysis from controlled studies is needed to examine comparative outcomes between surgical management techniques in patients with partial ACL injury in order to develop appropriate treatment guidelines.

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