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Current Trends in ACL Repair: Primary Repair, Mechanical Augmentation and Biological Supplementation

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Abstract

Anterior Cruciate Ligament (ACL) tear is one amongst frequent knee injuries. This injury is troublesome as it causes instability of knee while walking/running and also predisposes to the risk of early osteoarthritis in long run. So, its proper management is important, but has always remained debatable and controversial as well. Advancements in tissue engineering and regenerative medicine has changed the understanding of ACL's anatomy and it's healing potential and thus a renewed interest has emerged towards ACL repair again over the established gold standard "ACL reconstruction". Novel techniques like bridging with fiber tapes, Internal Brace Ligament Augmentation (IBLA), and Dynamic Intraligamentary Stabilization (DIS) have emerged focusing on mechanical strength. Also, supplements like bio-scaffolds, platelets & platelet rich plasma (PRP) are in the offing to aid biological ligamentous healing. We will present review of past practice, current trend and future prospects of ACL repair.

Keywords: Anterior Cruciate Ligament; Repair; Reconstruction; Augmentation; Supplementation.

Introduction

Anterior Cruciate Ligament (ACL) is the primary knee stabilizer that provides both anterior-posterior translational and rotational stability [1]. ACL is one of the frequently injured structure of knee [2] and it's estimated about 1,00,000 to 2,00,000 ACL ruptures per year in the United States alone, with an annual incidence of 1 in 3500 [3]. Tear of ACL (Figure 1) resulting in translational and rotational instability becomes a predisposing factor for meniscal injury, articular cartilage damage/degeneration [4] and risk of post-traumatic early osteoarthritis in long run [5]. So, proper management of this injury is very important, but the patterns of management of ACL tear has always remained debatable and controversial [6]. With advancement in medical sciences and sports injuries, the understanding of ACL anatomy and it's healing potential has changed too. Earlier, the ACL was thought to have poor healing potential and also high failure rates even after surgical repair. Thus, ACL reconstruction became "gold standard" and was widely adopted in practice [5]. But even with reconstruction, issues emerged like high cost of surgery [7], returning back to early sports activities in all [8], re-rupture and poor results after revision surgeries especially in sports persons [7, 9–11]. Recently, a renewed interest has emerged after improved knowledge of healing of ACL came up with advancements in tissue engineering and regenerative medicine [5]. Many basic sciences and clinical pilot studies are coming up showing improvements in retention of proprioception and native kinematics with ACL repair [5, 12]. But mechanical stability following primary repair is still a matter of concern. So, novel techniques have emerged focusing on mechanical strength like bridging with fiber tapes, Internal Brace Ligament Augmentation (IBLA), and Dynamic Intraligamentary Stabilization (DIS). Biologically enhanced repair supplements like use of bio-scaffolds, platelets & platelet rich plasma (PRP) are in the offing to aid ligament healing [12].

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History of ACL Repair

ACL injury was first diagnosed in military cadets based on physical examination [13]. Mayo-Robson performed the first primary ACL repair using catgut ligature and Battle published the first report [14]. Later, a 5 years follow up of 64 primary ACL repair by Feagin et al with open technique reported 50% failure and they mentioned ACL repair to be a compromising event [15]. In another study by Taylor et al, their 30 years follow up showed decreased activity levels of patients and an equal mix of acceptable and unacceptable outcomes [16]. Kaplan et al had 6 years follow up with 52 primary ACL repairs and only 17% failure was reported but 42% had abnormal laxity on KT-1000 test [17]. In the meantime, ACL reconstruction developed which showed promising results over primary repair. This was reported by several

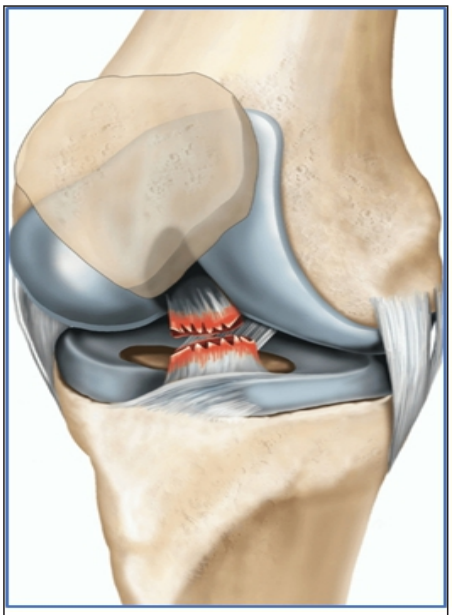

Figure 1: ACL tear (Healthdirect AustraliaTM)

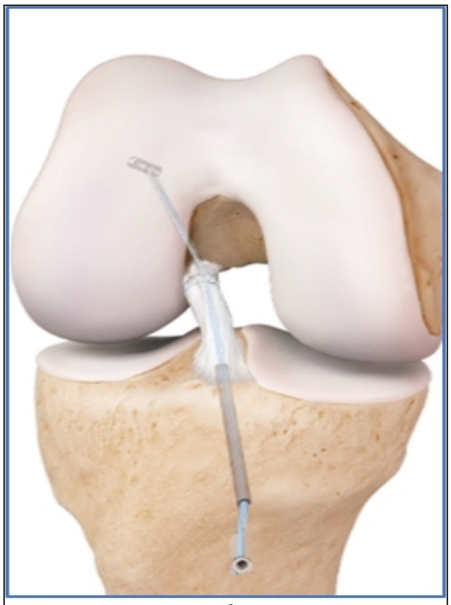

Figure 2: Internal Brace Ligament Augmentation (ArthrexTM)

randomized controlled trials [6, 18, 19] and eventually ACL reconstruction took over to ACL repair totally and became "gold standard" in ACL rupture management [12].

However, none of the RCT's has looked for "tear location". In 1991, Sherman et al illustrated that tear location has significant effect on outcome of primary repair of torn ACL. He showed that mid-substance tears and poor tissue quality has poorer results in comparison to proximal tears [20]. With advancements in functional tissue engineering and regenerative medicines, retention of proprioception and knee kinematics was illustrated which renewed the interest in revisiting ACL repair [5, 12].

Primary ACL Repair

Work in ACL repair started again from 2014 and till 2020 many advancements have been achieved. Easy access to MRI facility helped to diagnose the location of ACL tear in recent years and hence novel techniques of ACL repair emerged [12, 21]. On contrary, appropriate patient selection for primary ACL repair is another key feature for successful repair [22–24]. Palmer described multiple loop suture technique of primary repair in which both the proximal and distal stumps of torn ACL were tied with multiple loop sutures. Two holes were drilled at origin and insertion sites of ACL in femur and tibia, the sutures were passed thought it and tied sutures were tied over the bone bridge in 30 degrees of knee flexion [25]. There retains a benefit of no donor site morbidity in this technique. But Kaplan et al reviewed 52 repairs done via same technique and reported of 17% failure and 42% abnormal laxity of ligament [17]. Augmentations with free grafts like patellar tendon or quadriceps has been tried by many and the results were slightly better over primary repair alone [6]. Kennedy and co-workers [26, 27] developed Ligament Augmentation Device (LAD) and promising clinical results were reported by Schabus [28] who first used it. He felt that synthetic materials would protect repair till sufficient tissue growth and remodelling occurs [6, 28]. Based on these Engebrestsen et al suggested that repair alone should no longer be done [6].

After arthroscopic techniques evolved, 56 suture anchor based arthroscopic repairs was reported by Jonkergouw et al [29]. All of them were the repairs of proximal tears with a portion having suture augmentation. Overall patient outcome was improved but 10.7% repairs failed in 1 year and this was higher than that reported for ACLR. Even Nwachukwu et al reported evaluation on primary ACL repair [30]. However, all of these studies reported that it's the proximal tear that retains best chances of healing following repair and the chances of failure is still higher than ACLR [3].

Internal Brace Ligament Augmentation (IBLA)

In this augmentation system, a 2.5mm high strength polythethylene tape is used to bridge from anatomical attachments of mid-bundle portions of anterior cruciate ligament on both femur and tibia (Figure 2). To stimulate healing, multiple micro-fractures are carried out at femoral end. Recently IBLA is looked into as a potential solution to high failure rates reported previously with ACL repair. The hope is linked to the presumption that mechanical support by bracing may allow improved healing of ligament [12]. In literature, there are published case reports of sportsman returning to previous sports following ACL repair with IBLA and good rehabilitation [31]. Mackay et al in a case series with 1 year follow-up reported comparable outcome of IBLA repair with conventional ACL reconstruction and greatest improvement in return to early sports activities [32]. In another study of 2 years follow-up, Wilson et al reported excellent outcome with retained proprioception which may prevent re-injury and posttraumatic osteoarthritis development [33]. Heusdens et al reported its clinical relevance with proximal ACL tear repair [34] whereas Smith et al demonstrated its good clinical outcome following pediatric ACL repair [35].

Dynamic Intraligamentary Stabilization (DIS)

Developed in Berne, it shares the concept that protective mechanical environment aid with ligamentous healing [12]. It's

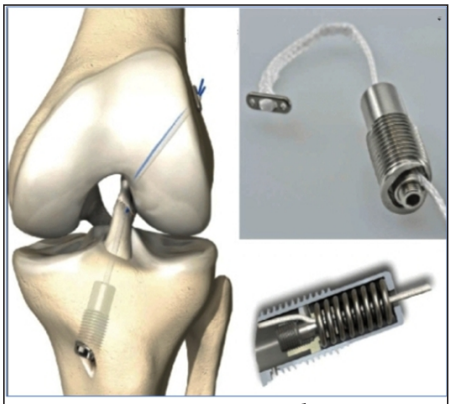

Figure 3: Dynamic Intraligamentary Stabilization (Mathys MedicalTM)

called dynamic as it contains a threaded sleeve with preloaded spring and mechanism for securing the spring in tibia. A braided polyethylene wire (1.8mm) passes via it through middle of torn ACL, and is attached both sides by tibial component and femoral endobutton (Figure 3). Extensive microfracture is performed at femoral end similar to IBLA [12].

Once applied, it provides a constant or posterior drawer force to proximal tibia allowing 8mm of excursion and ensuring continuous tension over entire range of movement. As shown by biomechanical studies, its capable of creating [21] and maintaining [36] sagittal plane stability throughout the rehabilitation. Thus, primary repair is secured even after allowing immediate full weight bearing postoperatively. DIS is recommended within 3 weeks of injury and this early surgical timing helps in meniscus preservation and also shorter absence from work [37]. In a matched study on return to work, Bieri et al [37] compared DIS and ACLR and found no significant difference between treatment cost, secondary arthroscopies, revision rates whereas early return to work was evident in DIS group. Thus, they recommended DIS as an additional treatment option in ACL tear. Henle et al [38] presented his experience of DIS with 3 years follow-up in 278 patients. He concluded that in majority of torn ACL, the anatomic repositioning along with DIS and micro fracture leads to clinically stable healing of torn ACL in majority. But studies also showed that DIS is not suitable for high level athletes [38] and there are high rates of implant removal (up to 50%) due to local discomfort [36] too. No clinical studies have directly compared DIS and ACLR in terms of proprioception or donor morbidity and even no objective or functional clinical improvement has been noted [12].

Biological Supplements

Even after augmentation of primary repairs with all these advanced techniques, 15% failure rate has been reported [15]. This makes us think that some room is still left for improvement. On the other hand the advancements in tissue engineering and regenerative medicine has changed the understanding of ACL's healing potential and thus a renewed interest has emerged towards use of biological supplements to enhance healing following ACL repair [5]. Augmentation with biological supplements in ACL repair has even shown promising results in experimental studies [39].

Bio-scaffolds

These are materials that have been engineered to cause desirable cellular interactions to contribute to the formation of new functional tissues. Hydrogels was one of initial forays to be used as carrier or growth factors due to their structural similarity to extracellular matrix of most connective tissues [40]. Hyaluronan is the another one used as intra-articular injection to deliver growth factor for ligament healing [41, 42], but no current literature support its use following ACL repair [12]. In a study by Robayo et al, tissue engineered collagen scaffolds has been used for ruptured ACL [43]. Colonisation of fibroblasts within implanted collagen scaffold was seen in their laboratory experiment. Joshi et al showed improved biomechanical and histo-chemical characteristics of repaired ligaments following augmentation with collagen platelet composite patches [44]. Further research into these bioscaffolds are actively being pursued [45].

Platelet Rich Plasma (PRP)

PRP retains 3 times the normal concentration of platelets in plasma and is gaining more attention into practice in recent years. It also contains growth factors like Platelet Derived Growth Factor (PDGF), Transforming Growth Factor (TGF) and Vascular Endothelial Growth Factor (VEGF) [46]. To increase collagen gene expression in fibroblasts, both platelets and plasma proteins are necessary [47]. ACL fibroblasts on getting exposed to PRP and peripheral blood mononuclear cells for 2 weeks, showed proliferation, gene expression and collagen production in a study by Yoshida and Murray [48]. Improved biomechanical and histological characteristics of repaired ACL in canine model was demonstrated by Murray et al in 2006 on using PRP in combination with a collagen scaffold [49]. However, the same author in 2009 showed that PRP doesn't enhance the strength of repaired ACL [44]. So, we can make it out from here that collagen scaffold enhances the effect of PRP. Yoshida et al [50] in 2014 and Fleming et al [46] in 2015 worked further on this combination method of bio-enhancement. They found that increased platelet concentration has inhibitory effect on collagen gene expression and also increased cell apoptosis. Thus, they advised that optimum platelet concentration for excellent cell growth and gene expression needs to be identified to create a better solution for ligamentous healing.

Stem Cells

The mesenchymal stem cells (MSCs) of ACL are closely located near blood vessels and within collagenous structures of the tissue. They resemble in characteristics to the bone marrow stem cells (growth pattern, morphology,

osteogenic and adipogenic capacity) but they differ somehow. The MSCs of ACL have less proliferation and chondrogenic capacity [51]. Ge et al showed that MSCs promote type I and III collagen production within the ligament when added to scaffolds or ACL grafts [52]. Zhang et al compared the MSCs of ACL with that of medial collateral ligament (MCL) and showed that the ACL stem cells have slower growth rates and differential potential than stem cells of MCL [53]. Here ACL was taken as intra-articular ligament and MCL as extra-articular ligament.

In a pre-clinical study by Figueroa et al, complete regeneration of ligament was seen in 1 of 3 ACLs having primary repair with collagen bio-scaffold and MSCs at 12 weeks [54]. These bio-enhanced repairs with PRP/MSCs/bioscaffold has even comparable biomechanical properties to ACL reconstruction [55]. Further works are going on and we hope that biological augmentations will have a role in ACL healing following repair.

Conclusion

Though ACL reconstruction is an established gold standard in treatment of ACL injury, renewed interest has emerged in "ACL repair" due to illustration of proprioception and knee kinematics retention following repair by recently advancing tissue engineering and regenerative medicine works. Tear location has significant effect on outcome of primary repair and the proximal tears are considered best for it. Augmentation with free graft, synthetic graft, augmentation devices and biological supplements shows even better results than primary repair alone. But there are still lots of questions unanswered regarding biomechanical strength, repair failures and the benefits in athletes. This opens avenues for further work and exploration to establish benefits of ACL repair over reconstruction.

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