Return to sport following anterior cruciate ligament reconstruction: the argument for a multimodal approach to optimise decision-making: current concepts

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ABSTRACT
Existing literature is varied in the methods used to make this determination in the treatment of athletes who have undergone recent anterior cruciate ligament (ACL) reconstruction. Some authors report using primarily time-based criteria, while others advocate for physical measures and kinematic testing to inform decision-making. The goal of this paper is to elucidate the most current medical evidence regarding identification of the earliest point at which a patient may safely return to sport. The present review therefore seeks to examine the evidence from a critical perspective—breaking down the biology of graft maturation, effect of graft choice, potential for image-guided monitoring of progression and results associated with time-based versus functional criteria-based return to play—to justify a multifactorial approach to effectively advance athletes to return to sport. The findings of the present study reaffirm that time is a prerequisite for the biological progression that must occur for a reconstructed ligament to withstand loads demanded by athletes during sport. Modifications of surgical techniques and graft selection may positively impact the rate of graft maturation, and evidence suggests that imaging studies may offer informative data to enhance monitoring of this process. Aspects of both functional and cognitive testing have also demonstrated utility in prior studies and consequently have been factored into modern proposed methods of determining the athlete’s readiness for sport. Further work is needed to definitively determine the optimal method of clearing an athlete to return to sport following ACL reconstruction. Evidence to date strongly suggests a role of a multimodal algorithmic approach that factors in time, graft biology and functional testing in return-to-play decision-making following ACL reconstruction. Level of evidence: level V.

INTRODUCTION
The optimal method to return athletes to play following anterior cruciate ligament (ACL) reconstruction is currently unclear.1–8 Despite attracting substantial research attention, wide variation exists in the criteria employed by orthopaedic sports medicine physicians.1,4,9,10 The breadth of decision-making processes employed by medical providers implies that the most effective algorithm to return athletes to play in a safe yet efficient manner is as yet unknown.

Biology of graft maturation is thought to represent a key factor, and consequently time from injury and surgery is commonly referenced as a primary criterion.11–13 However, graft maturity has been demonstrated to be significantly affected by multiple factors, including graft type and source, in addition to time since reconstruction.14–20 Although many authors have cited this biological basis for returning athletes to play at predetermined time points, others have advocated for greater use of muscular and kinematic testing to make such decisions.9,10,18,21–23 Others have started to investigate
the utility of incorporating imaging that demonstrate correlation with graft strength into such decision-making algorithms. To date, however, mixed results have been published that demonstrate support for the use of each method without clear or consistent superiority of any. As a result, return to sport following ACL reconstruction remains controversial. The goal of the current review is therefore to analyse the evidence on return to play after ACL reconstruction with a focus on the biology of graft maturation, incorporation of functional tests, role of imaging, influence of graft choice, and the pros and cons of time versus functional testing criteria as the basis for return-to-sport decision-making.

METHODS
The 2020 ISAKOS Symposium regarding the optimisation of return-to-play decision-making algorithms for patients who have undergone ACL reconstruction was reviewed extensively. Relevant publications cited in the symposium were identified and findings were included where pertinent.

Included were articles which (1) discussed primary ACL reconstruction and (2) contained basic science or clinical data relevant to the predefined categories of interest. These were (1) biology and graft maturation, (2) imaging assessment, (3) functional testing, (4) graft choice, and (5) time versus criterion. Excluded were articles which (1) discussed revision ACL reconstruction, (2) focused on patient age <10 or (3) did not present data relevant to the above-mentioned categories.

Outcome measures of interest included time to return to play, retear rates, patient-reported outcomes, graft strength and histological findings. All evidence were analysed with the goal determining the earliest possible time to safely return athletes to sport.

Biology and graft maturation
Much of the initial basis for time-based return to play originates from a landmark publication by Clancy et al. on ACL and posterior cruciate ligament (PCL) reconstructions. They found that patellar tendon grafts showed increases in vascularity and collagen organisation and continued remodelling at 3, 6, 9 and 12 months. In their animal model, load to failure increased from 52% at 6 months to 81% at 12 months.

However, Clancy et al.'s work and much of the early data on the postoperative experience of grafts were obtained from animal studies. Later data reported that at 8 months postoperatively a patellar tendon autograft demonstrated 87% of the strength of a native ACL. This was substantially higher than that previously reported for the same time point in animals.

Since the publication of these studies, other authors have expanded the knowledge base on the time course of the progression experienced with grafts. Jackson et al. demonstrated key differences in the rate of biological incorporation and duration of inflammatory response that are tied to the source of the graft itself. Multiple other studies have identified maximum pull-out strength at 8–12 weeks for tendon-to-bone healing and 6–8 weeks for bone-to-bone, shedding light on the ingrowth process. More recent data relevant to descriptions of the intra-articular graft maturation process as involving an early healing phase with central necrosis and hypocellularity, followed by a proliferative phase with remodelling and revascularisation. Finally, a lamination phase occurs around 6 months postreconstruction and involves modifications in collagen fibres to ultimately yield a structure more similar to a native ACL.

Recent work has been done to capitalise on this expanded biological knowledge base relevant to ACL reconstruction surgery. Specifically, attention has been turned to technical modifications that may augment the rate or efficacy of the ligament maturation process. For example, histological and mechanical data on the incorporation of a periosteal flap with graft placement suggest that employing the technique results in greater insertion strengths in shorter times. Maintaining remnant tissue of the torn ACL similarly appears to cause some biological changes—as demonstrated by differential gene expression profiles—although the clinical effect is not yet certain and may increase the risk of developing ‘Cyclops lesions’.

Orthobiologics for the purpose of healing augmentation have also been recently explored. Use of fibrin clot has been shown to result in greater vascularity and tissue maturity within the intra-articular segment of grafts at various time points. Use of platelet-rich plasma (PRP) has potential as well. A recent review found that PRP was associated with significantly quicker graft maturation in four studies and trended towards significance in two others. In this subset of publications, however, consistent improvements in clinical outcomes were not identified. Nevertheless, these early data points suggest potential for accelerating timelines for return to activity that are otherwise limited by the inherent biology of the graft maturation process.

Imaging assessment
The differences in mechanical strength known to be associated with each of the biological phases of graft progression suggest potential utility of imaging studies to identify stages of graft maturation. Panos et al. have taken the first steps towards incorporating such knowledge by creating a time-based model using pooled data from multiple studies to clarify the trend of signal intensity over time.

According to their findings, a high signal on T2 MRI of grafts from 6 weeks to 4 months postoperatively corresponds to a fibroblastic proliferative phase, and a low-signal intensity on T2-weighted images between 6 and 12 months postoperatively corresponds to histological maturation of the graft, as noted by improved collagen fibril alignment and increased vascularity. Models predicting graft maturity were significantly affected by multiple factors, including graft type, source and time since reconstruction. Incorporating the effects of such variables would be essential if using imaging to evaluate the maturity of grafts. To date, imaging changes have not been clearly correlated with ligament strength, which remains a central criticism of the argument to employing costly studies in routine postoperative evaluation.

However, a relatively logical argument in favour of incorporating MRI into return-to-sport algorithms can be made. The clearly downsized is added resource utilisation. Nevertheless, as imaging modalities evolve and potentially lead to more cost-effective solutions, understanding the correlation of magnetic resonance appearance with histological stages of graft lamination may become increasingly valuable in assessing patients for their ability to safely increase their levels of activity.
Functional testing

Harris et al found in their 2014 systematic review that most level 1 randomised controlled trials failed to incorporate functional testing into their return-to-sport decision-making. However, some relatively recent evidence suggests a potential benefit of doing so and provides scientific support for its role in activity advancement algorithms.4 5 15 32 51

The existing literature strongly supports the utility of single leg squat and drop vertical jump, focusing specifically on trunk stability, frontal plane knee valgus, hip rotational moments, pelvic tilt and comparison with the contralateral leg as relevant parameters of interest. 3 49 54-60 Performance on various forms of hop testing (single hop, triple hop and crossover hop testing) has similarly been strongly associated with reduced risk of reinjury. 5 34 56-60 The Y-balance test is commonly described as a test employed in the athletic clearance process after ACL reconstruction as well, but it appears to be less directly supported. 20 22 29 34 56 38 61 Still, evidence does suggest its role in identifying asymmetry between limbs, which is a highly relevant factor. 22 30 54 56-58 61 62 Multiple authors have shown that symmetrical quadriceps strength prior to returning to sport protects against retear, and Nawasreh et al in 2018 demonstrated an association with a patient’s ability to return to preinjury level of activity.22 23 37-40

Still, no consensus exists on the optimal battery of functional testing exercises needed to assess athletes for their ability to return to sport. However, there is evidence to support testing in general. In a study of 158 professional athletes who returned to sport after ACL reconstruction, retear rates were 4.1 times higher in the subset who did not meet the criteria on six functional tests, including running T tests, single hop, triple hop and crossover hop tests, and isokinetic strength testing at 60°, 180° and 300°.10 This highlights an opportunity for medical providers to intervene at a point when a significant difference can be made on the clinical outcome of an athlete.

Multiple authors have also found that patient-reported outcomes (the Knee Outcome Survey-Activities of Daily Living and the Global Rating Scale of Perceived Function) were predictive of return to preinjury activity, and Werner et al found that such measures were actually more predictive than any functional performance measures.23 30 In combination, these works lend support to incorporating psychological testing to guide progression from one rehabilitation stage to the next, as proposed by van Melick et al.28

Multiple algorithms have been proposed with various muscular and psychological testing criteria.1 3-6 10 23 28 30 51 63 A meta-analysis by Webster and Hewett29 in 2019 of functional testing prior to return to sport found a relatively low passing rate of 23% at 6 months postoperatively among 18 studies of functional testing criteria after ACL reconstruction. Equivocal results were associated with passing such testing, with some reports finding decreased graft rupture rates and others identifying no differences, highlighting potential room for improvement.29 In most models, progression generally is proposed to occur through stages guided initially by level of impairment. Subsequently, advancement in sport-specific training and finally return to play is proposed. However, validating studies have yet to be performed and are of obvious importance to providing definitive recommendations.

Graft choice

Graft source is known to affect the maturation process of a reconstructed ACL and is consequently a consideration in return-to-play algorithms.9 11 25 Work from Jackson et al13 39 demonstrated key differences between implanted patellar tendon allograft and autograft tissue in a goat model. Specifically, allografts show slower biological incorporation, prolonged inflammation and fewer small-diameter collagen fibrils at 6 months postoperatively compared with autografts.13 39 These manifested clinically as differences in anterior-posterior translation and force to failure in favour of the autograft tissue, and additional studies since have confirmed that patients treated with autograft recover over a different time course compared with their allograft counterparts.13 39 Some studies suggest greater frequency of return to sports with autografts over allografts, but not necessarily faster return according to existing literature.64

As discussed previously, bone-to-bone healing occurs at a faster rate than tendon-to-bone healing and represents one of the major points of distinction between graft types.7 11 16 18 20 25 26 38 39 Additionally, imaging models similarly have identified differences in signal intensity when comparing patellar tendon and hamstring autografts, thereby suggesting differences in graft maturity that may affect the safety of a patient returning to physical activity.11 16 18 20 25 34 38 Specifically, low MRI signal has been shown to occur in hamstring autografts during the first postoperative year and correlates with relatively static remodelling over this time.11 16 18 20 25 34 38 Patellar tendon autografts, on the other hand, yield increased MRI signal during the first year, which correlates with cellular and tissue changes observed at the histological level.11 16 18 20 25 34 38

Mixed results have historically been reported when comparing hamstring and patellar tendon autografts and effects on return to play. Clear differences between graft types have not been consistently demonstrated, but recent evidence from secondary analysis of the ACL-SPORTS trial data suggests that hamstring tendon autograft may result in earlier satisfaction of return-to-sport criteria.65 These criteria, which were primarily based on quadriceps strength symmetry, hop testing and patient-reported outcomes, were met at an average of 32 weeks postoperatively by the hamstring cohort compared with 45 weeks by the patellar tendon cohort.

Multiple studies have identified graft choice as a potential risk factor for early failure, and some have identified differential survivorship based on graft selection.9 11 25 Xie et al 38 in their 2014 meta-analysis identified what likely represent important differences in pivot shift and ability to return to preinjury levels of sport between graft types. They additionally identified a trend towards a difference in laxity measurements, but this did not reach the threshold for statistical significance.38

DISCUSSION

Ultimately, the question is whether time-based or functional criteria-based return to play is associated with improved outcomes. While some evidence suggests decreased injury rate as return to sport is delayed, this has not universally held true.3 4 5 7 8 10 30 33 Research on National Football League athletes, for example, has demonstrated that while failure did tend to occur most commonly in the early return period, there was no correlation found between time and likelihood of failure.62

Time offers the benefit that it is relatively easy to understand and similarly straightforward to study for research purposes. The biological progression of graft tissue requires a certain amount of time itself, thereby providing a basis for clearance using this logic.11 12 16 18 20 25 34 38 However, criteria-based return to play can be better customised to athletes’ specific needs for his or her sport. Although a spectrum of criteria have been proposed...
for consideration, it is important to consider the applicability of what is being measured.

Some published studies have found a protective effect of criteria-based return to play, as discussed previously.1–6 10 23 28 30 33 63 However, with a meta-analysis of 18 studies reporting that only 23% of athletes achieved passing status at 6 months postoperatively, this calls into question whether such criteria are informative in isolation or whether their effects are confounded by time.29 Nevertheless, evidence to date suggests a potential benefit of incorporating functional criteria that can be applied to and customised for individual athletes prior to returning them to sport.6

As a result, multiple proposals for evidence-based progression of rehabilitation and return-to-play clearance have been published, and many provide a logical basis for incorporating cognitive measures in addition to physical testing.5–8 10 18 23 30 33 However, definitive recommendations cannot be made based on the existing literature alone. Ultimately, the key remains to identify when a reconstructed ACL is actually strong enough to withstand functional loads, which will likely be specific to individual patients and movement patterns. While other factors will remain relevant, substantial evidence exists to suggest that both time and functional testing can inform such an assessment.

Improving the collective understanding of the effects of modern technical modifications on the amount of time needed for grafts to mature would better inform such recommendations as well. Currently, the optimal return-to-play algorithm following ACL reconstruction likely employs a multifactorial approach considering time, functional testing criteria and cognitive measures together.

CONCLUSION

The optimal algorithm employed by orthopaedic surgeons to guide recommendations on returning to sports in athletic patients following ACL reconstruction remains unclear. Time is a prerequisite for the biological progression that must occur for a reconstructed ligament to withstand loads demanded by athletes during sport. Modifications of surgical techniques and graft selection may positively impact the rate of graft maturation, and evidence suggests that imaging studies may offer informative data to enhance monitoring of this process. Aspects of both functional and cognitive testing have also demonstrated utility in prior studies and consequently have been factored into modern proposed methods of determining the athlete’s readiness for sport. Further work is needed to test and validate such proposals, but evidence to date suggests roles for all of the above in the form of a multimodal algorithmic approach to return-to-play decision-making after ACL reconstruction.

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Current concepts review


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