

THE FUTURE OF SCIENCE IN A FIELD OF SHORT HISTORY

WHICH DIRECTION TO GO IN HAMSTRING RESEARCH?

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INTRODUCTION

Hamstring injuries are among the most prevalent sports injuries, yet we are still faced with a lack of scientific knowledge on this topic. Despite the growing number of publications over the last 3 decades, our current knowledge on aetiology, prognosis and therapy is based on only 1000 published injuries. If we restrict ourselves to level 1 trials, then there are less than 200 injuries examined.

Compared to 3 decades ago, our research has led to limited progress for the individual athlete: the injury and re-injury rate has not changed. In contrast, in medical conditions like Diabetes mellitus, millions of subjects

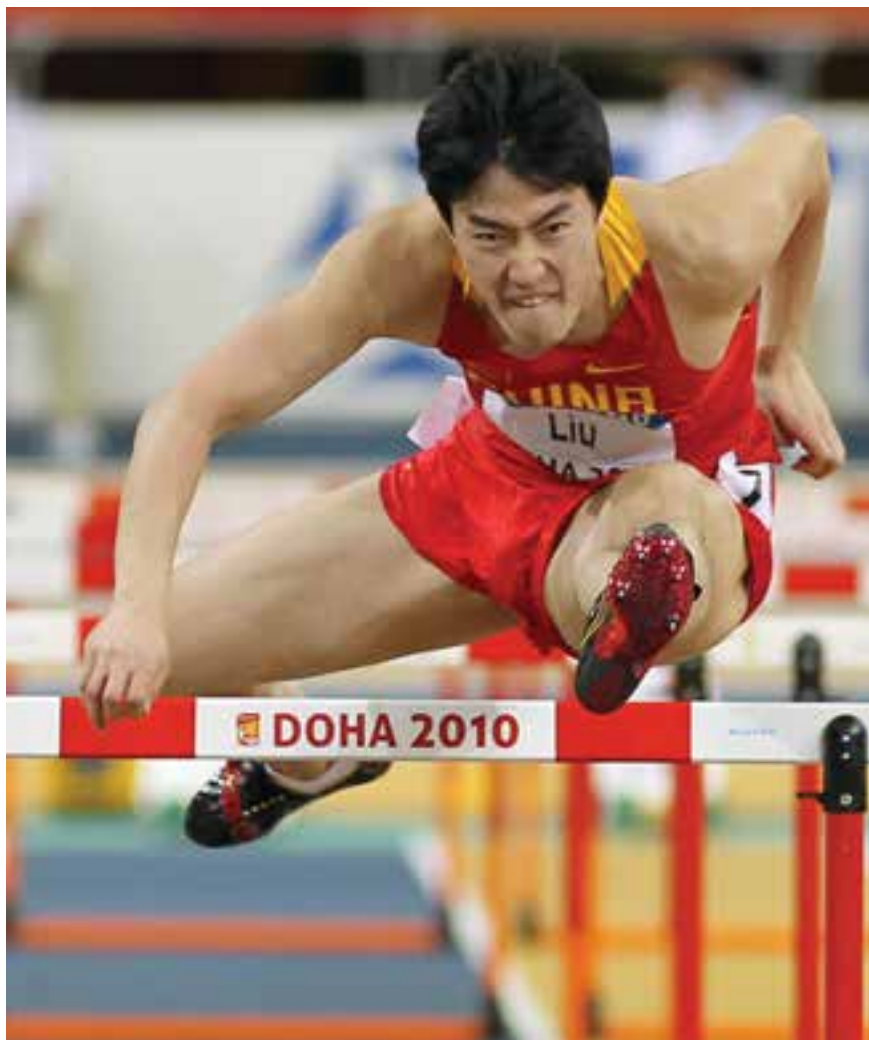
have been described in the scientific literature. Even with the strong history of research in that area, these conditions are still the subject of on-going research as many questions have not yet been answered. The relatively short history of hamstring science places our challenges in perspective and should guide us to strengthen our academic base toward a brighter scientific future.

RISK FACTORS / PREVENTION OF HAMSTRING INJURIES

The Nordic hamstring exercise is very effective in preventing hamstring injuries in soccer¹. However, we are still left with a number of issues: in order to prevent one

new injury, 25 players need to do the exercise pre-season as well as during the season, at a certain level of intensity with the resultant significant time demands. If ankle, ACL, groin and other areas are also injury problems that need preventive attention, when do we find the time to play ball?

If we identify those players with a previous hamstring injury, we need only three players to do the full Nordic hamstring programme to prevent one injury. But we want to avoid the new injuries as well. The injuries that still occur despite the Nordic hamstring programme could be injuries with another aetiology than the one targeted by the programme.



It is assumed that the main action of the programme is the eccentric strengthening of the hamstrings muscles and that this increased strength prevents predominantly the sprinting type of hamstring injury. However, hamstring injuries which appear different on imaging might also have a different injury mechanism, and actually may be quite different from each other. Although this prevention programme is quite effective and superior to most sports injury preventive programmes, it is still not ideal and not targeting all assumed aetiologies.

Furthermore, the reason that the Nordic hamstrings are effective in preventing hamstring injury is not clear. Research into this might help develop the programme further and perhaps help delineate the types of acute posterior thigh pain (including

their aetiology and pathology) that are not affected by the exercise programme.

As we will discuss later, we are still using very clinical, overly simplistic terms (sprinting and stretching types of injury) and sports medicine's understanding of the aetiology and pathology of hamstring injuries remains at a very basic level. In this context, the similarity to the current state of knowledge in the area of groin injuries is obvious: the lack of understanding of the complex muscular actions about the pelvis and its adjacent joints. More detailed differentiation of hamstring injuries could allow for identification of risk factors that are specific to certain types of injuries, and thus we might be able to identify methods to prevent the injuries that are not reduced by the Nordic hamstring exercise programme. This will, however, demand

very high numbers of injuries, and therefore large multicentre or database studies should be considered internationally.

TOO SHORT HISTORY FOR UNDERSTANDING THE INJURY MECHANISM

It is generally assumed that hamstring injuries occur as a cause of excessive eccentric action (sprinting type injury) or passive lengthening (stretching type injury) of the muscle. This frequently-cited assumption is based on only two case series in sprinters² and dancers³ and has not been reproduced. The actual mechanisms of injury are probably more complex than this practical, relevant classification. Kicking, for example, is a commonly reported injury mechanism, comprising both eccentric loading and outer range lengthening of the hamstring and matches with both suggested injury mechanisms.

From biomechanical studies there is some evidence for eccentric loading during the terminal swing phase as a possible injury mechanism during sprinting. However, there are only two cases described in which a hamstring injury occurred during sprinting analysis in a research setting^{4,5}. The increased availability of high quality recordings by (high speed) cameras in elite sports might offer an opportunity to study large numbers of injury situations and correlate these with clinical and imaging features. Although this will probably give us some insight into the possible mechanisms, it will always represent an indirect observation of what actually happened at a microscopic level.

New innovative imaging techniques should provide insight into muscle injury mechanisms. We dream of high speed, wireless, mobile, skin-attached ultrasound techniques to catch that single injury moment. That futuristic tool will give us the answer of whether the terminal swing phase is indeed the mechanism of injury.

ATHLETES ARE ONLY INTERESTED IN THE NEAR FUTURE

After being injured, the first question of the athlete, coaching staff and press is: 'when can he/she return to play (RTP)?' Although our knowledge has improved at a group level, previous research has not satisfactorily answered this question for the individual athlete. Multiple clinical and MRI parameters have been shown to correlate with time to RTP. Although these prognostic factors are valuable for scientific studies, its limited strength of correlation and variability of time to RTP makes it unsuitable for accurately predicting the time to RTP for an individual athlete.

For example, in the largest series on the prognostic value of MRI, Ekstrand et al⁶ found that in professional football players, MRI grading was significantly correlated with injury time. This group found, for each grade injury (in days \pm standard deviation):

- Grade 0: 8 \pm 3;
- Grade I: 17 \pm 10;
- Grade II: 22 \pm 11;
- Grade III: 73 \pm 60 days.

However, by applying these results to an individual athlete with a grade I hamstring injury, we can estimate that there is a 95% chance that he returns to play within 0 to 37 days (mean 17 days \pm two times the standard deviation of 10 days). The athlete, coaching staff and press will argue that it is a long way from being a satisfactory estimation of the injury time.

A great challenge for future research is to provide tools which can give a more accurate prediction of injury time. The first step in this research is to identify the relevant prognostic factors. However, as hamstring injuries are a complex multifactorial condition, only by combining multiple prognostic factors for injury duration in mathematical models will we ever be able to provide accurate predictions for the individual athlete. Designing and validating an ultimate prognostic model requires a multitude of standardised documented hamstring injuries. To answer the athlete's most important and simple question we are forced to build up a worldwide online hamstring injury registration system.

RETURN TO PLAY DECISION-MAKING

It is a major challenge to decide whether an athlete can safely RTP. The high re-injury rate (up to 63%) reflects this challenge. The re-injuries have been reported predominantly (59%) to occur in the first month after RTP^{7,8}. Although there is no consensus, in clinical practice an

athlete is typically regarded as being ready once full range of motion, full strength and functional sport specific activities (e.g. sprinting, jumping, cutting) can be performed asymptotically. Despite this conventional approach, the decision of functional, physiological and psychological readiness remains challenging.

The ultimate test of whether an athlete is ready to RTP is to mimic the use and loading of the injured muscle as required during (match) play itself. However, failing this ultimate test implies that the athlete suffers a re-injury. Less rigorous tests will reduce the risk of re-injury during testing, but there will always be an uncertainty on the athlete's readiness to RTP. Basic science shows that healing of the injury is incomplete at the time clinical tests indicate recovery and that the majority of athletes can RTP successfully prior to complete tissue healing^{9,10}. A conservative approach of waiting for complete tissue healing would probably decrease the re-injury rate, but might unnecessarily extend the RTP.

As stated by Orchard et al^{9,10} RTP management strategies should not aim at re-injury risk elimination, but at re-injury risk evaluation to support RTP decisions. The practical decision-based RTP model of Creighton et al¹¹ guides us through three steps:

- **Step 1:** medical factors such as age, injury history, psychological state, outcome of clinical tests and imaging are evaluated.
- **Step 2:** sport-specific risk modifiers such as type, level of sport and player position are evaluated.
- **Step 3:** decision modifiers such as timing in season, importance of match (e.g. final), external pressure and financial conflicts of interest are considered.

Future research should aim at validation of the medical factors and sport risk modifiers to provide mathematical models that can accurately predict re-injury risk to guide RTP decision-making after hamstring injury. For example, based on multiple factors such as patient characteristics (e.g. age, gender, previous injuries), injury characteristics (e.g. mechanism, location, extent) and clinical tests (e.g. flexibility, strength, functional field testing), the future ultimate model estimates that a player has a 6% risk of being re-injured when

sports medicine's understanding of the aetiology and pathology of hamstring injuries remains at a very basic level

participating in the upcoming match and 2% in the second game. The decision to RTP in the upcoming match will differ whether it is a World Cup final or a pre-season friendly game. Although this model does not provide definitive RTP criteria, it provides an evidence-based risk estimation that fits in a decision-based RTP approach.

FUTURE IMAGING TECHNIQUES

Dynamic MRI

Conventional MRI presents a static image, thereby ignoring the dynamic contraction mechanics of the muscles. Dynamic MRI can measure motion of muscles under different loading conditions. Future studies using dynamic high resolution MRI can study the musculotendinous morphology and mechanics during contractions and will provide a better insight into contraction mechanics and association with injury risk¹².

Diffuse tensor imaging

Diffuse tensor imaging (DTI) is an advanced MRI-technique that images detailed muscle fibre structure. DTI measures the movement of water molecules in tissue. In healthy muscle tissue water molecules move more easily along the muscle fibres than in other directions. At the site of muscle fibre disruption the movement of water molecules is changed (Figure 1). A preliminary study in marathon runners showed that DTI could detect even the lowest grade of muscle fibre disruption due to delayed onset muscle soreness which could not be detected by conventional MRI¹³. DTI therefore has great potential for quantifying muscle damage and monitoring tissue healing.

NEW INNOVATIVE THERAPIES: THE FUTURE

Platelet-rich plasma

There is increasing interest in the sports medicine and athletic community about providing endogenous growth factors directly to the injury site to potentially facilitate healing and earlier RTP after musculoskeletal injury. Probably the most popular therapy that has been recently introduced is the injection of platelet rich plasma (PRP). PRP is derived from centrifuging whole blood and then separating out of the platelets. The platelet concentration in PRP is dependent on the

separation technique, and is typically two to six times higher than that of whole blood. PRP is the cellular component of plasma that settles after centrifugation and contains numerous growth factors.

Basic research studies have shown that myoblasts can be proliferated by growth factors like b-FBG, IGF-1 and NGF. In deliberately injured animal muscles, these growth factors are seen to be essential for increasing regeneration. The platelet derived growth factors are stored in α -granules found within platelets, and are released in a selective manner upon activation. These growth factors are assumed to provide the regenerative benefits of PRP. Despite the promising results from basic research, and apparent widespread clinical use, there is a lack of high-level evidence of randomised

clinical trials assessing the efficacy of PRP in treating muscle injuries.

Currently, two high-level randomised controlled trials on PRP in hamstring injuries are near completion (at Aspetar – Qatar Orthopaedic and Sports Medicine Hospital and in the Netherlands). The results of these studies can be expected soon and will provide the required clinical evidence about the efficacy of this popular and promising therapy for muscle injuries.

Stem cells

Another innovative therapy that has potential for future treatment in muscle injuries is the use of stem cells. Basic research has shown that muscle-derived stem cells have the potential to promote muscle tissue repair after injury by increasing

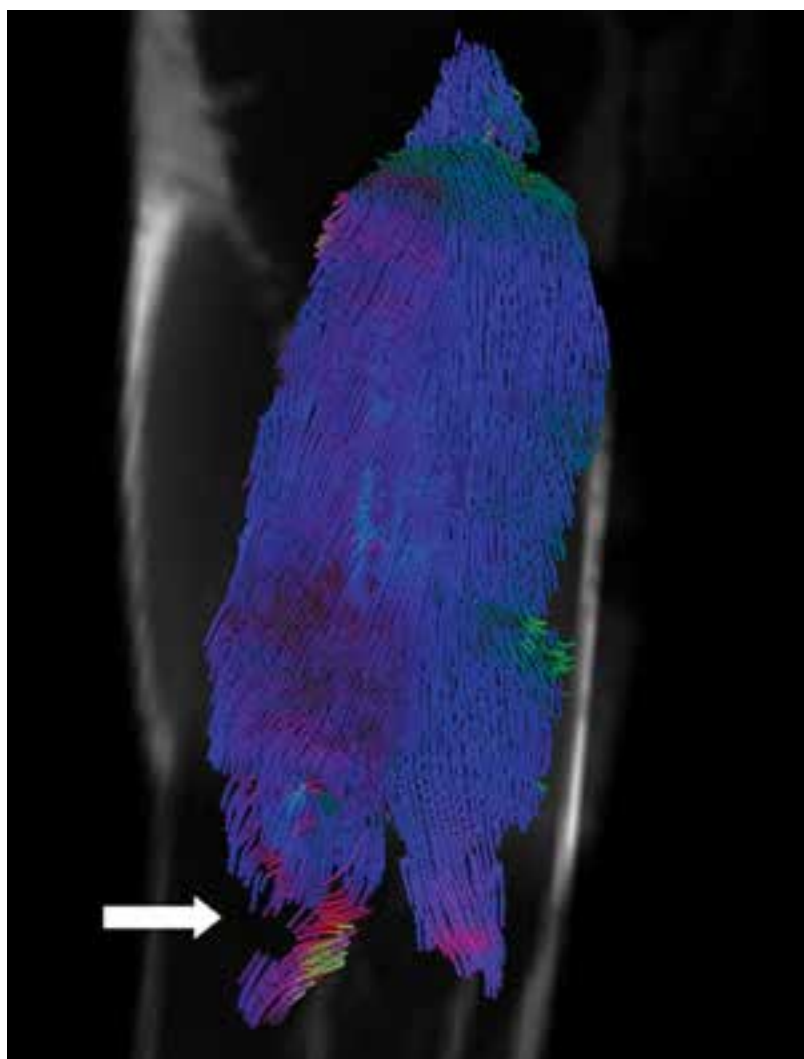


Figure 1: Image obtained by diffuse tensor imaging showing a distal m. biceps femoris rupture (arrow).

“Our most experienced sports physicians will have had managed just 150 hamstring injuries in his/her 30-year career”



angiogenesis and reducing scar tissue formation¹⁴. These stem cells are assumed to produce biologically active signals (cytokines or other signalling molecules) that elicit a response in donor cells and host cells leading to neovascularisation, chemo-attraction of host cells to the injury site and recruiting host cells to participate in the muscle tissue repair.

Future basic and clinical research are required to illuminate the mechanism of action and the effects of stem cell therapy in muscle injury before clinical application can be considered. Although clinical application of stem cell therapy in muscle injuries should not be expected in the near future, we suspect that it has great therapeutic potential in regeneration of injured muscle tissue.

Anti-fibrotic agent Losartan

MRI studies of athletes with hamstring injuries showed that in approximately 1/3 of the injuries, fibrous tissue developed (Reurink et al, unpublished data) and persisted on the long term¹⁵. Although

clinical studies are lacking, the formation of fibrous/scar tissue is frequently reported as a risk factor of re-injury as it alters the mechanics of muscle tissue. Therapeutic interventions are frequently aimed at preventing/reducing scar tissue formation.

Basic science has indicated that TGF- β 1 plays a key role in the formation of fibrosis. Inhibiting the TGF- β 1 expression results in reduced fibrosis¹⁴. The angiotensin II receptor blocker losartan has been suggested as a potential anti-fibrotic agent by its regulating effect on the TGF- β 1 signalling pathways. In a mouse model, histological analysis showed lower fibrous tissue formation in mice treated with losartan compared to controls¹⁶. Reports of clinical application of losartan in hamstring injuries are limited to only two cases, however.

Although fibrosis is frequently reported as a risk factor for re-injury and anti-fibrotic agents may potentially reduce the formation of scar tissue, there is still no clinical evidence that fibrous tissue is associated with an increased re-injury risk. Before research into these agents develops,

this link needs to be clearly established. If fibrosis does increase re-injury risk, placebo-controlled randomised clinical trials are then needed to assess efficacy of anti-fibrotic agents in treating muscle injuries.

NUMBERS NEEDED TO BUILD UP EVIDENCE AND HISTORY

Our main limitation is that, as individual sports physicians, we deal with a too few hamstring injuries to justify an experienced-based approach. For example, in professional football, with five injuries per team per season, our most experienced sports physicians will have had managed just 150 hamstring injuries in his/her 30-year career. In contrast, a single general practitioner manages over 3,000 Diabetes mellitus cases in his/her career.

As a consequence, to gain expertise and to answer the most important and simple questions we need to collaborate. Faced with our short research history, a worldwide hamstring registration system should start today rather than tomorrow.



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