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A short review

Basic science and clinical studies coincide: active treatment approach is needed after a sports injury

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The basic response to injury at the tissue level is well known and consists of acute inflammatory phase, proliferative phase, and maturation and remodeling phase. Knowing these phases, the treatment and rehabilitation program of athletes' acute musculoskeletal injuries should use a short period of immobilization followed by controlled and progressive mobilization. Both experimental and clinical trials have given systematic and convincing evidence that this program is superior to immobilization – a good example where basic science and clinical studies do coincide – and therefore active approach is needed in the treatment of these injuries.

Acute injuries, usually in forms of meniscal injuries, chondral damages, contusions, muscle-tendon strains, ligament sprains and related ruptures, are common in sports and exercise. Without proper diagnosis and treatment these injuries may seriously risk the participation in training and competition. Also, the injury may become chronic thus interfering with, or even stopping, the career of the athlete. Thus, it is not surprising that people in sports medicine have put lots of interest and efforts in discovering ways for faster and better healing of the injury, and in this respect, the question of post-injury immobilization vs. mobilization has received growing attention in both experimental and clinical science. The aim of this short review is to summarize the current immobilization–mobilization literature and authors' long-term scientific and clinical experience in this area.

Normal tissue response after an injury

A prerequisite for efforts to speed up and improve healing after a soft-tissue injury is to understand the normal tissue response after the injury. This response has been studied in detail and a rather good consensus exists that it includes three overlapping phases: (1) the acute inflammatory phase (about days 0–7), (2) the proliferative phase (about days 7–21), and (3) the maturation and remodeling phase (about days 21 and over) (Järvinen, 1976a,b; Noyes, 1977; Ogata, Whiteside, Andersen, 1980; Järvinen & Lehto, 1993; Buckwalter, 1995; Kannus, 2000; Kääriäinen, Liljamo, Pelto-Huikko, Heino, Jarvinen, Kalimo, 2001). In the *acute post-injury phase*, cell membrane damage, plasma leakage, and subsequent (reactive) vasoconstriction, ischemia and metabolic disturbance lead to reaction of inflammation, which consists of tissue edema, fibrin exudation, infiltration of the inflammatory cells (leukocytes, monocyte–lymphocyte line cells, and macrophages), production of fibronectin, capillary wall thickening, and capillary occlusions. Clinically, inflammation manifests as swelling, erythema, increased temperature, pain, and loss of function. The process is mediated by vascular, cellular and chemical events finally resulting in tissue regeneration and repair, or in a more non-optimal case, chronic, degenerative tissue and scar and adhesion formation (Järvinen, 1976a,b; Noyes, 1977; Järvinen & Lehto, 1993; Buckwalter, 1995; Jozsa & Kannus, 1997; Buckwalter & Grodzinsky, 1999; Kääriäinen, 2001).

In the *proliferative phase*, characteristic changes are fibrin clotting and proliferation of fibroblasts, myofibroblasts, synovial cells, and capillaries. The migration and proliferation of these cells is stimulated by the presence of growth factors produced from platelets and macrophages (Tidball, 1995; Chan, Fu, Qin, Lee, Rolf, Chan, 2000). The inflammatory cells eliminate the damaged tissue fragments by phagocytosis, and production of fibronectin and collagens (first the weaker, thin type III collagen and then type I collagen, the basic collagen of the musculoskeletal tissues) and

other extracellular matrix components (proteoglycans and matrix glycoproteins) by the fibroblasts is extensive and clearly increased (Järvinen, 1976a,b; Jozsa & Kannus, 1997). Thus, towards the end of the proliferative phase, the original fibrin clot becomes gradually replaced by a more permanent structure called granulation tissue (Jozsa & Kannus, 1997; Kääriäinen, 2001).

In the *phase of maturation and remodeling*, the proteoglycan-water, cell, and capillary content of the healing tissue gradually decreases and the type I collagen fibers start to reorganize themselves into normal orientation. About six to eight weeks after the injury, the new collagen fibers begin to withstand stress rather well, although it has to be remembered the basic observation that entire maturation period of healing collagenous tissue (tendons, ligaments) may be long, up till one to two years (Noyes, 1977; Ng et al., 1997).

Basic science requirements for treatment and rehabilitation

Relying on the above described basic-science knowledge on connective tissue healing, an ideal treatment and rehabilitation program of an acute soft-tissue injury has been formulated to fulfill four requirements (Järvinen, 1976a,b; Noyes, 1977; Salter, Hamilton, Wedge, 1984; Kannus et al., 1992a,b; Järvinen & Lehto, 1993; Kannus, 2000). Firstly, immediately after the injury and till about day 7, the injured tissue should be treated with *the RICE principle*: rest, ice, compression, and elevation. This minimizes pain, swelling, inflammation, and hemorrhage, to offer the best possible conditions for the healing process (Noyes, 1977; Jozsa & Kannus, 1997; Salter et al., 1984).

The second requirement is *protection and immobilization* of the damaged tissue area. This is important during the first one to three weeks after the injury. Protection is needed to prevent additional bleeding to the injury site, secondary injuries (re-ruptures), and early distension and lengthening of injured structures (Kannus & Järvinen, 1987; Kannus, 2000), while immobilization is followed by optimal fibroblast differentiation and invasion in the injured area that results in undisturbed production of collagen fibers (Järvinen, 1975, 1976b; Järvinen & Lehto, 1993). In this phase, mobilization of the damaged tissue too early and intensively may result in re-ruptures and weaker tissue (seen as immature granulation tissue via prolonged type III collagen and fibronectin formation) than that produced during an optimal period of immobilization (Järvinen, 1975, 1976b; Hurme, 1991; Järvinen & Lehto, 1993).

Thirdly, approximately two-three weeks after injury, collagen maturation and remodeling initiate (Järvinen & Lehto, 1993; Jozsa & Kannus, 1997) and this phase can be enhanced by *controlled mobilization* (less injured parts of the tissue or joint can be mobilized earlier, often already during the proliferative phase of healing) and, perhaps even more importantly, all parts of the musculoskeletal system (muscles, tendons, ligaments, chondral tissues, and bones) must avoid the deleterious effects of extended immobilization (Noyes, 1977; Häggmark & Eriksson, 1979; Akeson, Amiel, Woo, 1980; Ogata et al., 1980; Jozsa, Järvinen, Kannus, Reffy, 1987; Jozsa, Reffy, Järvinen, Kannus, Lehto, Kvist, 1988; Kannus et al., 1992a,b; Järvinen & Lehto, 1993; Buckwalter, 1995; Buckwalter & Grodzinsky, 1999; Kannus, 2000; Orchard & Best, 2002). Controlled muscle stretching and joint movement improve the orientation of collagen fibers parallel with the stress lines of the normal collagen fibers and they can prevent the tissue atrophy caused by immobilization (Järvinen, 1976a, b; Kannus et al., 1992a).

Fourthly, about six to eight weeks after the injury the new collagen fibers begin to withstand the tensile stress well and there are no pathophysiologic reasons to continue protection any longer (Kannus et al., 1992a,b). The rehabilitation is thus directed towards quick and complete return to exercise and sports.

Experimental and clinical studies

Examining then the evidence for (or against) the above noted basic science requirements on optimal treatment and rehabilitation of any type of acute soft-tissue injury (cartilage, ligament, muscle, or tendon) the *experimental literature* speaks strongly for the use of early, controlled mobilization instead of prolonged immobilization (Buckwalter, 1995; Buckwalter & Grodzinsky, 1999; Kannus, 2000). In other words, the authors have not found systematic experimental evidence to support the concept that immobilization would result in better outcome than early mobilization. Two examples (cartilage, muscle) are given below:

Experimental immobilization of an animal joint has been shown to be detrimental to *cartilage tissue* (Akeson et al., 1980; Salter et al., 1984; Arokoski, Jurvelin, Väätäinen, Helminen, 2000), and therefore, a consensus exists that post-injury or post-operative immobilization should be minimized in the treatment of cartilage lesions (Buckwalter, 1995; Messner & Roos, 2000). Continuous passive motion, though inconvenient for the patient, probably provides the loading conditions necessary for the new cartilage to produce matrix-specific proteins as well as suppresses the catabolic effects of post-injury inflammatory reaction on the cells of the joint, as shown in many *in vitro* studies (Messner & Roos, 2000; Salter et al., 1984; Agarwal, Long, Gassner, Piesco, Buckley, 2001; Long, Gassner, Agarwal, 2001). However, after a cartilage injury no method of repair or rehabilitation has yet been shown to be able to produce structurally and functionally normal neocartilage (Messner & Roos, 2000).

Concerning the *healing process of muscle injuries,* investigations from the universities of Tampere and Turku, Finland have first studied in detail the normal phases of healing of an experimentally injured rat gastrocnemius muscle, and then, the effects of early mobilization vs. immobilization on this process (Järvinen, 1975; Järvinen, 1976a,b; Hurme, 1991; Järvinen & Lehto, 1993; Rantanen, 1995; Kääriäinen, Järvinen, Järvinen, Kalimo, 2000a,b; Kääriäinen, 2001; Kääriäinen, Järvinen, Kalimo, 2001). These studies have shown that in a shearing type of muscle injury both myofibers and the surrounding connective tissue framework are ruptured and thereby the functional tendon–muscle–tendon unit disrupted. They have also demonstrated that the healing phase of muscle injury consists of two simultaneous processes: (a) regeneration of the disrupted myofibers and nerves; (b) formation of a connective tissue scar (Järvinen & Lehto, 1993; Kääriäinen et al., 2000a,b, 2001). In the early phase of normal healing (which is equivalent to about the acute inflammatory phase and early proliferative phase of the classic trauma response), the stumps of the ruptured myofibers become joined together via a loose connective tissue scar, through which the ends of regenerating myofibers then start to pierce. During the early phase of healing, the regenerating fibers also form integrin-mediated lateral fiber-to-fiber adhesions to compensate the lost connection at the rupture site (Kääriäinen et al., 2000a,b, 2001).

The above noted process of healing of an experimentally injured rat gastrocnemius muscle goes on until about day 14 post-injury, whereafter the opposite ends of the regenerating myofibers begin to attach to the interposed extracellular scar matrix by new mini-myotendinous junctions so that function of the entire muscle becomes again possible. At the same time, the additional integrin-mediated lateral adhesions of the myofibres start to disappear and a complementary increase in dystrophin and dystrophin associated molecule-complex take place on the lateral sarcolemmas (Kääriäinen et al., 2000a,b, 2001). The opposite muscle stumps appear to remain attached to (and separated by) the interposed scar tissue for many months, and it is also possible that in some situations, the original muscle may become permanently divided into two consecutive functional units separated by the permanent scar tissue between them (Kääriäinen et al., 2000a,b).

Then, according to the above noted dissertation studies, normal muscle fiber regeneration is often inhibited by the formation of pathologic, dense connective scar tissue. Although immobilization following injury limits the size of the connective tissue area formed within the site of injury, the connective tissue does not mature properly (i.e. does not regain the mechanical strength), penetration of new muscle fibers into the connective tissue is poor, and the neofiber orientation is complex and not parallel with the uninjured muscle fibers (Järvinen, 1975; Lehto, 1983; Hurme, 1991; Rantanen, 1995; Kääriäinen, 2001). In addition, immobilization for longer than one week is followed by marked general atrophy of the injured gastrocnemius muscle as well as substantial production of intramuscular connective tissue between the healthy muscle fibers (Kannus et al., 1992a, 1998). Mobilization started immediately after injury is, in turn, followed by a dense scar formation in the injury area prohibiting regeneration of the muscle fibers (Järvinen, 1975, 1976b; Järvinen & Lehto, 1993).

The best overall result is achieved when mobilization is started after a short period of immobilization (3–5 days in a rat gastrocnemius muscle) (Järvinen, 1976a,b; Järvinen & Lehto, 1993; Buckwalter, 1995; Kääriäinen, 2001). In this model, where the injured rat muscle is first immobilized for a short period of time and then adequately mobilized, penetration of the new muscle fibers through the immature connective tissue seems to be at its best and the orientation of these regenerated muscle fibers is aligned with the uninjured muscle fibers. Also, the gain in strength and capacity for energy absorption has been similar and as good as that of muscles treated by early mobilization alone (Järvinen & Lehto, 1993; Kääriäinen, 2001). The basic principles of these animal experimental findings are probably well applicable to muscle injuries of humans, although the time frame of healing can be different: in humans, the healing time is likely to be longer than that in small animals (Orchard & Best, 2002).

Finally, the results of *controlled clinical trials in humans* have supported those of the above noted experimental studies by giving evidence that a carefully conducted early controlled mobilization is better than immobilization – not only in the primary treatment of acute soft-tissue injuries but also in post-operative care (Buckwalter & Grodzinsky, 1999; Kannus, 2000). The superiority of the former has been shown to be especially clear in terms of quicker recovery and return to activity; however, without jeopardizing the subjective or objective long-term outcome. Evidence for early mobilization is available for many types of injuries, such as *ankle ligament ruptures*, *knee ligament tears*, *articular cartilage injuries*, and *Achilles tendon ruptures* (Häggmark & Eriksson, 1979; Salter et al., 1984; Zwipp et al., 1986; Sandberg et al., 1987; Kannus & Renström, 1991; Saleh et al., 1992; Eiff et al., 1994; Holch et al., 1994; Thermann et al., 1995; Zwipp, 1995; Kaikkonen et al., 1996; Karlsson et al., 1996, 1999; Mortensen et al., 1999). In *elbow or shoulder dislocations and non-displaced bone fractures*, early mobilization has also given very good results (Connolly, 1998; Stoffelen & Broos, 1998; Ross et al., 1999; Egol et al., 2000). Future controlled clinical studies should focus on those injuries and anatomic sites, in which knowledge is most limited.

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