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REVIEW ARTICLE

Effects of and Response to Mechanical Loading on the Knee

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Abstract

Mechanical loading to the knee joint results in a differential response based on the local capacity of the tissues (ligament, tendon, meniscus, cartilage, and bone) and how those tissues subsequently adapt to that load at the molecular and cellular level. Participation in cutting, pivoting, and jumping sports predisposes the knee to the risk of injury. In this narrative review, we describe different mechanisms of loading that can result in excessive loads to the knee, leading to ligamentous, musculotendinous, meniscal, and chondral injuries or maladaptations. Following injury (or surgery) to structures around the knee, the primary goal of rehabilitation is to maximize the patient's response to exercise at the current level of function, while minimizing the risk of re-injury to the healing tissue. Clinicians should have a clear understanding of the specific injured tissue(s), and rehabilitation should be driven by knowledge of tissue-healing constraints, knee complex and lower extremity biomechanics, neuromuscular physiology, task-specific activities involving weight-bearing and non-weight-bearing conditions, and training principles. We provide a practical application for prescribing loading progressions of exercises, functional activities, and mobility tasks based on their mechanical load profile to knee-specific structures during the rehabilitation process. Various loading interventions can be used by clinicians to produce physical stress to address body function, physical impairments, activity limitations, and participation restrictions. By modifying the mechanical load elements, clinicians can alter the tissue adaptations, facilitate motor learning, and resolve corresponding physical impairments. Providing different loads that create variable tensile, compressive, and shear deformation on the tissue through mechanotransduction and specificity can promote the appropriate stress adaptations to increase tissue capacity and injury tolerance. Tools for monitoring rehabilitation training loads to the knee are proposed to assess the reactivity of the knee joint to mechanical loading to monitor excessive mechanical loads and facilitate optimal rehabilitation.

Key Points

Mechanical loads encountered during high-risk cutting, pivoting, and jumping sports predispose the structures of the knee to risk of injury.

Individual tissues of the knee respond and adapt differently to various mechanical load stimuli.

Appropriate selection of exercises, functional activities, and mobility tasks based on their mechanical load profile can be utilized during rehabilitation to systematically and progressively load the structure of the knee to promote tissue healing and repair.

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1 Introduction

The knee is one of the most commonly injured joints in sports [1], particularly vulnerable during activities that involve cutting, pivoting, and jumping [2]. Hence, sports such as soccer, volleyball, basketball, team handball, and alpine skiing report the highest incidence of knee injuries [3, 4]. These aforementioned activities place varied and substantial loads upon the knee that can result in injury to several common structures [5, 6].

Mechanical loading can be described as the physical forces that act on or create a demand on the body at the systems level, anatomical structures at the organ and tissue level, and down to the molecular and cellular level [7]. These force variables involved in mechanical loading can be characterized by the magnitude, duration, frequency, rate of force development, and nature and direction of force application (Fig. 1). Figure 2 visually depicts the specific variables of magnitude, duration, frequency, and rate of force development that provide the mechanical stress and strain to trigger tissue adaptation [8]. These force variables interact with one another and create a variety of biomechanical loading patterns on the body and tissues, which can result in positive adaptations, such as increased tissue strength and structural load tolerance, or negative adaptations, such as acute stress-related, acute strain-related, or chronic overload injury [9]. Those positive adaptations typically occur through a biomechanically oriented intervention via physical training by varying mechanical loads to improve tissue capacity and mitigate injury risk [10, 11]. In regard to knee injuries, injuries to the ligaments, menisci, tendons, cartilage, and bone are the result of a complex interplay of tissue-specific strength and load tolerance, tissue-specific stress and strain, and force variables [9]. We discuss the different loading patterns that occur at the knee that can potentially result in tissue failure and injury.

Intra-articular and extra-articular ligaments provide passive joint stability during knee motion, with the anterior cruciate ligament (ACL) the most commonly injured knee ligament during sports [3, 4, 6] such as basketball, football (American and Australian Rules), soccer, volleyball, and team handball [12, 13]. The majority of ACL injuries are due to a non-contact mechanism that likely occurs during deceleration and acceleration motions from excessive quadriceps contraction and reduced hamstring co-contraction with the knee at or near full extension, [14] whereby ground reaction forces are transferred to the knee when the knee is in excessive knee abduction and tibial internal rotation during knee flexion [15, 16]. Anterior cruciate ligament loading was higher during any of these situations: (1) knee flexion angle less than 30° in combination with higher hip flexion and lower ankle plantar flexion angles from initial contact to peak knee flexion during landing [17] or a cutting/pivoting maneuver, [18] (2) application of a quadriceps force when combined with knee internal rotation, (3) a valgus load combined with knee internal rotation, or (4) excessive valgus knee loads applied during weight bearing (WB), decelerating activities [14, 18]. Most alpine ski-specific ACL mechanisms of injury are the consequences of an attempted recovery from a slip-catch [19]. Combined passive external force imparted on the tibia from the ski boot and an internal rapid force development from quick knee flexion, tibial internal

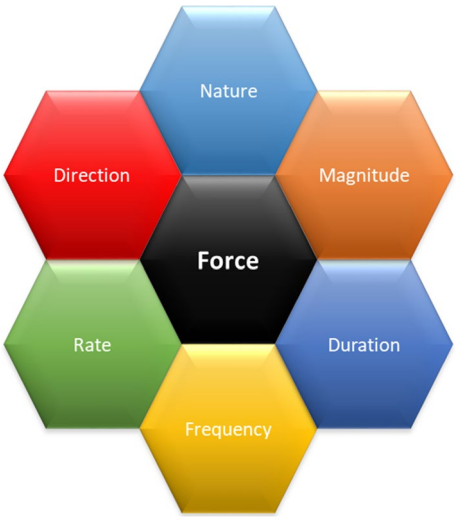

Fig. 1 Force variables

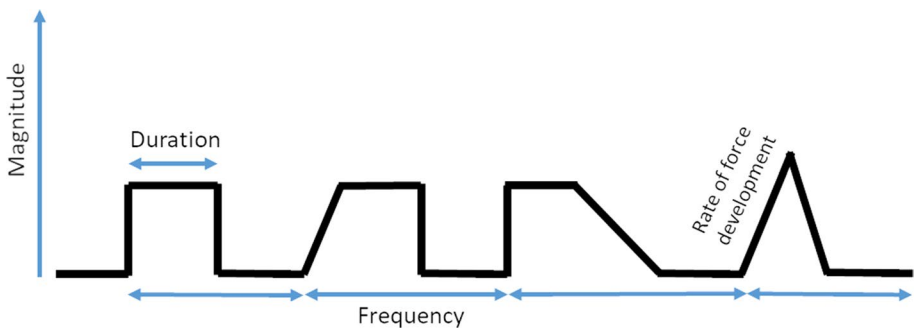

Fig. 2 Force variable characteristics

rotation, and knee valgus motion during a slip-catch results in higher shear forces directed to the ACL [19].

Injuries to the patellar tendon are common in sports. While traumatic ruptures can occur to the patellar or quadriceps tendon, these injuries are largely degenerative disorders that usually occur in sports with frequent explosive jumping [20]. Between 30 and 45% of volleyball and basketball players will develop patellar tendinopathy [21, 22]. Tendinopathy can result from microdamage and altered cell/matrix response due to abnormal loading [23]. Loading magnitude on the patellar tendon appears to be an important factor in the etiology of patellar tendinopathy [24–26]. Higher accumulated and acute workloads have been found to be associated with a higher injury risk in elite youth footballers, with the greatest risk of non-contact injury associated with high-speed running distances [27]. The risk of injury in athletes increases with rapid changes in training load, and a progressive, gradual, and systematic increase in training loads may be indicated to help mitigate non-contact injury risk [28].

Meniscus injuries are the second most common injury to the knee, with a prevalence of 12–14% and an incidence of 61 cases per 100,000 persons [3]. A high incidence of meniscal tears occur concomitantly with ACL injury, ranging from 22 to 86% [29]. Younger active individuals are more likely to sustain traumatic meniscus injuries, such as longitudinal or radial tears [30], which occur in the same sports with a predisposition for ACL injuries [31]. Similar cutting and pivoting mechanisms increase the axial and torsional forces on the meniscus, likely leading to traumatic meniscus tears [32].

With respect to articular cartilage lesions, 32–58% occur as a result of a traumatic, albeit non-contact injury mechanisms [33, 34]. Direct blunt trauma, indirect impact loading, or torsional loading are the primary mechanisms of injury to articular cartilage [35]. These mechanisms of injury produce high loading rates with increased magnitudes of loading. Low compressive strain along with high loading rates can cause decreased chondrocyte viability, and increasing compressive strain with high loading rates can lead to progressive severe cartilage lesions [36–38].

While post-traumatic osteoarthritis can develop after a knee injury and can be influenced by mechanical loading, it is beyond the scope of this review to discuss the pathogenesis of post-traumatic osteoarthritis. Buckwalter et al. [39] have provided an excellent review on the impact of mechanical loading on the development and progression of post-traumatic osteoarthritis.

These examples highlight how mechanical loading from sports participation can result in devastating and potentially career-ending injuries. Knowing how mechanical loads on knee joint tissue can result in injury, clinicians can leverage that knowledge to develop rehabilitation management strategies to help with tissue loading and healing. This aim of this review is to synthesize the current evidence around the importance of mechanotransduction and the effect of mechanical loading on the structural tissues of the knee joint. It also provides an overview of how these mechanical processes, encountered during daily, recreational, and sports activity, should be considered in the rehabilitation of patients following knee injury.

2 General Tissue Response to Mechanical Movement and Loading

The mechanical properties and physiological function of a tissue determine its strength and load tolerance or capacity. The load capacity of a tissue is dependent on the type and status of that tissue, and clearly varies between individuals. Local tissue or structure-specific load capacity is the "specific structure's ability to withstand tissue-specific cumulative load" [40]. Normal tissue has greater capacity to tolerate and adapt to load than pathological tissue. Tissue structures of young people have greater capacity than those of older people [41], and elite athletes require greater tissue capacity than recreational athletes [42], likely as a result of the interaction between activity-specific load capacity and structure-specific load capacity [43].

Mueller and Maluf proposed the "Physical Stress Theory" based on how biological tissues adapt to physical stress, and this has been expanded on by Dye with the envelope of function model [42, 44]. Biological tissues exhibit five adaptive responses to physical stress: (1) decreased stress tolerance (atrophy), (2) maintenance (homeostasis), (3) increased stress (hypertrophy), (4) injury, and (5) death [44] (Fig. 3). Applied physical stress below that required for tissue homeostasis may promote tissue atrophy (zone of subphysiological underload), while those in excess can promote tissue hypertrophy (zone of supraphysiological overload) [44]. However, if the physical stresses are too high (above the supraphysiological overload) and/or too frequent, resulting in inadequate recovery, injury and structural failure are likely to occur [44].

The envelope of function reflects the capability of the knee (or any joint or musculoskeletal system) to transfer a range of loads over a given period of time, but to do so while still remaining uninjured at the molecular or cellular level (i.e., while still maintaining tissue homeostasis) [42]. The relative relationship between these thresholds is fairly consistent between people, whereas the absolute values for thresholds vary greatly [44]. Multiple variables that contribute to cumulative load, such as magnitude-related, distribution-related, and capacity-related components, can influence the envelope of function [40]. Activity-specific loading that is applied progressively and systematically, along with the above components, can result in a shift in the

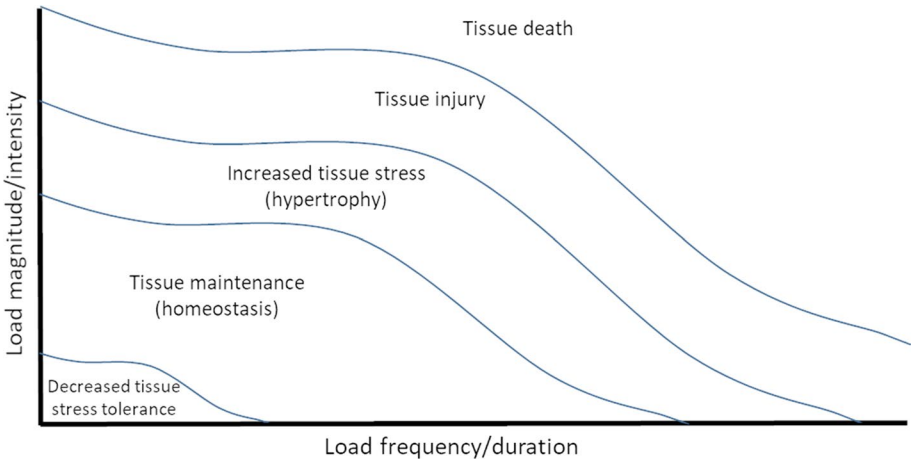

Fig. 3 Adaptive response to load

envelope of function, improving the activity-specific capacity and thereby enhancing tissue structure-specific capacity [10, 43]. The activity-specific loading (or stimulus) should be a greater-than-normal demand (overload) to initiate a stress response and challenge tissue homeostasis [44–46]. Repeated or chronic disruption of homeostasis leads to adaptations, which then requires even greater stimuli to further disrupt the newly required tissue capacity, resulting in even greater adaptations [45, 46]. However, if activity-specific loading remarkably surpasses structure-specific capacity, injury risk vastly increases [10, 11, 43] and tissue failure can occur [10, 11].

A tissue is at an activity-specific capacity when movement can be performed at an activity-specific load (magnitude, intensity, volume, and frequency) needed to perform and withstand the demands of training and competition without overt tissue damage or exacerbation of symptoms [28, 43, 47]. In order to better understand the tissue's capacity to tolerate load, we have expanded on several models to clarify the understanding of how the structure-specific tissue responds and adapts to load (Fig. 4) [9, 11, 28, 40, 48–51]. The physiology of individuals with the non-modifiable and modifiable determinants, along with tissue-specific strength, dictate the predisposition of a tissue to load response (Fig. 4A). External factors, such as playing conditions, surface-shoe interface, and other competitors, can elevate the tissue to be susceptible to injury when a load is applied [11]. As discussed previously, multiple components of the external load interact with the susceptible tissue of the knee (Fig. 4B).

Each structure in the knee has a unique stress–strain profile, which responds differently based on the type of mechanical stimulus (Fig. 4C). These adaptations can occur at the molecular, tissue, and organism levels, with external mechanical stimuli that load musculoskeletal tissues subsequently transmitted at the cellular level [52, 53]. These mechanical stimuli commonly are: (1) tension, (2) compression, (3) shear, (4) hydrostatic pressure, (5) vibration, and (6) fluid shear [52, 53]. Mechanotransduction is described as "the processes whereby the cells convert physiological mechanical stimuli into biochemical responses" [54]. Mechanotransduction can promote structural changes to different tissues (Table 1) [23, 54–57]. Depending on the type of tissue and the ability of that tissue to withstand those forces, modifications can occur at the cellular level that can alter extracellular matrix synthesis or degradation [53]. This can then influence tissue mechanical properties. Thompson et al. [53] provide a more detailed review of mechanotransduction at the cellular and molecular level.

Once a load is acutely applied to the tissue, for example, during a bout of training or exercise, the tissue initially has reduced capacity due to microstructural alterations in that tissue (Fig. 4C). This triggers a host of biochemical and gene expression responses from mechanosensitive cells (fibroblasts, endothelial cells, osteocytes) [52]. With adequate recovery following that activity load, tissues remodel via extracellular matrix synthesis [52, 53] and homeostasis is restored, at a higher capacity and with an improved performance potential (Fig. 4D). If the timing of the next load exposure is at the optimal point, the cycle is repeated with an additional increase in load capacity of the tissue. However, if the timing of the next load is too low or delayed, then improvement in load capacity is likely to not occur (Fig. 4D) [58]. If the time of the next load and subsequent loads is too high or soon with inadequate recovery, this can also trigger biochemical and gene expression responses from mechanosensitive cells. This can lead to extracellular matrix degradation [52, 53], likely resulting in reduced tissue capacity (Fig. 4D) or fatigue of the tissue. If mechanical loads grossly exceeded the capacity of the tissue that is already reduced or fatigued, this increases the risk of tissue failure or injury (Fig. 4D). The capacity of the tissue can then influence the individual physiology and predisposition of the tissue and how it responds to the next load. For further literature on

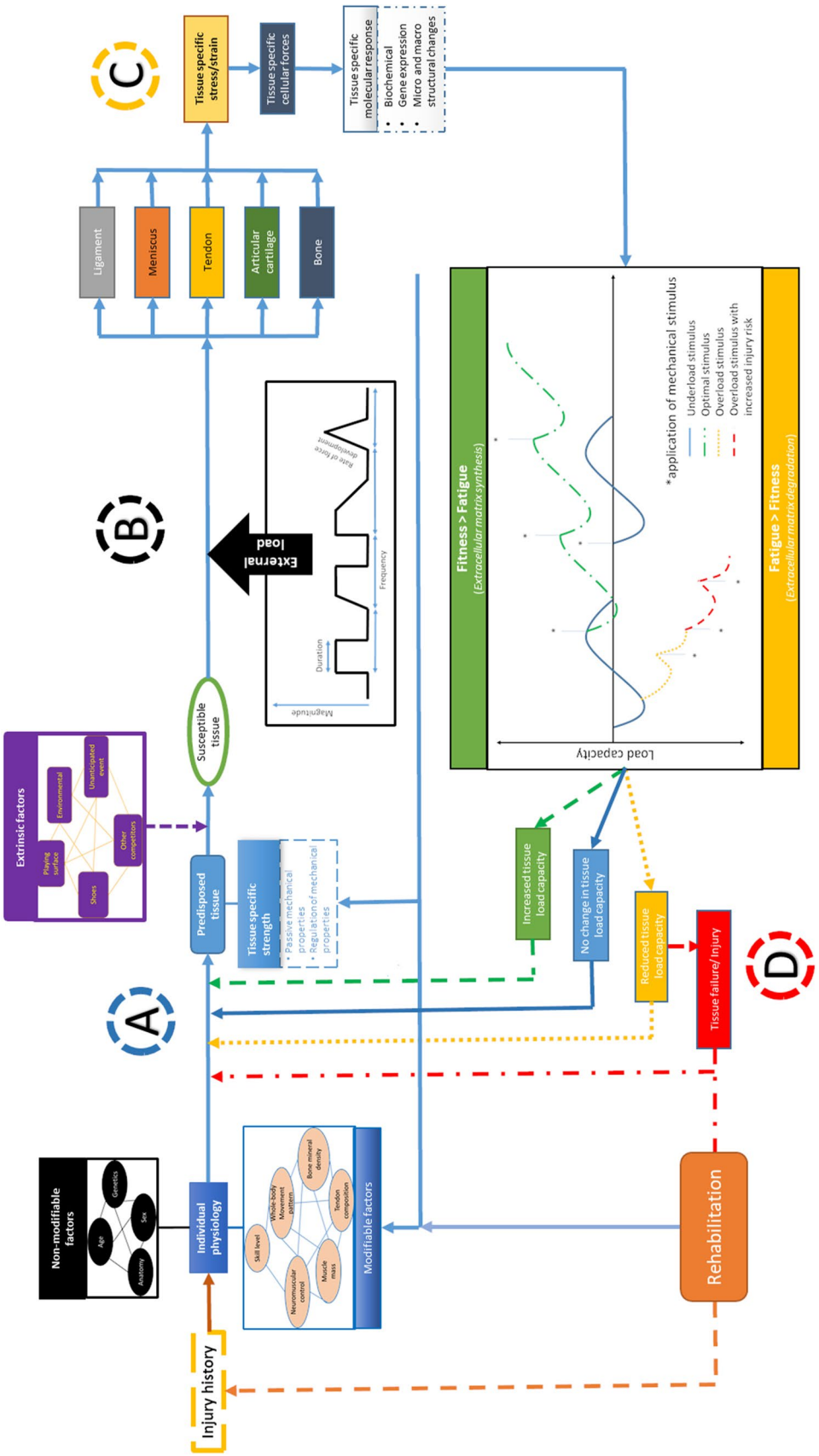

Fig. 4 A conceptual model for tissue structure-specific adaptations to an external load

Table 1 Tissue structure-specific and cell and molecular responses to mechanical stimuli

Tissue	Mechanical stimulus	Stress/strain	Cell and molecular response	Positive tissue response (appropriate loads)	Negative tissue response (overload or underload)
Ligament	↑ Tension	Cyclic, below tissue failure	Fibroblasts activate collagen, proteoglycan, other protein content	↑ Tissue mass ↑ Mechanical stiffness ↑ Load to failure over time	
Tendon	↑ Tension from muscle		Tenocytes build the extracellular matrix, including collagen, fibronectin and proteoglycans	↑ Tissue cross-sectional area ↑ Mechanical stiffness ↑ Blood flow	
Meniscus	↑ Compression (axial load)		Fibrochondrocyte metabolism		Disuse atrophy
Articular cartilage	↑ Compression (axial load) ↑ Shear	Cyclic, below tissue failure	Chondrocyte metabolism influenced by matrix and cell deformation, hydrostatic and osmotic pressure, fluid flow, and altered matrix water content, ion concentration and fixed charge density	↑ Cartilage thickness ↑ Surface area ↑ Cartilage volume ↑ Cartilage deformation capacity	↓ Cartilage thickness Adhesions Fibrillations, fissures, ulceration Altered aggrecan Altered collagen synthesis
Bone	↑ Compression (axial load) ↑ Tension ↑ Shear ↑ Hydrostatic pressure	↑ Strain Uneven load distribution Cyclic with short periods of reduced loading	Osteocytes respond via ion channels, integrins and the cytoskeleton, gap junctions and hemichannels, and primary cilia Osteocytes differentiate into osteoblasts Osteoblasts <> osteoclasts	↑ Cortical bone thickness ↑ Bone mineral density ↑ Vascularization	Altered cortical bone thickness Altered bone mineral density

↑ increased, ↓ decreased

the adaptations of tissue to physical stress, the reader is referred to Mueller and Maluf [44]. The next sections discuss how knee-specific tissues (ligament, tendon, meniscus, cartilage, and bone) respond to loads and how those tissues subsequently adapt to that load. We will discuss these tissue-specific responses in subsequent sections.

2.1 Ligament Response to Loading

Ligaments are composed of about two-thirds water, and the remaining third collagen including several amino acids, by weight [59]. When dry ("dry weight"), collagen accounts for about three-quarters of total weight, and the remaining quarter is made from proteoglycans, elastin, and even less from other proteins and glycoproteins. The collagen is primarily made from type I collagen (about 85%), and type III collagen [59, 60]. Microscopically, the collagen bundles have a cross-linked pattern of parallel fibers that have a zig-zag pattern in form, likely to allow them to undergo tension loads while elongating without damaging the structural properties [59, 61]. In between those collagen fibers are fibroblasts that regulate the extracellular matrix. These fibroblasts help to regulate metabolism within the ligament, especially important during loading. Proteoglycans, which are also in the extracellular matrix, bind water and support the viscoelastic nature of the ligament [62]. The ability of ligaments to lengthen when under tension and then return to their original shape is due to their viscoelastic nature. However, without offloading the ligament (i.e., "creep"), over a prolonged period, the ligament may be unable to return to the original length [62, 63]. The following is a discussion of the effects associated with loading on a ligament.

Like many tissues of the body, the ligament adapts to sub-failure tension loading. Ligaments exposed to cyclic loading, below failure, demonstrate increased mass, stiffness, and load to failure over time [61]. Loading of ligaments leads to enhanced cellular synthetic and proliferative effects, increased strength, size, matrix organization, and collagen content. When tension is beyond the strength of the ligament (supraphysiological loading), there is tissue failure on a partial or complete scale. During the proliferative and repair phases following loading, fibroblasts are activated to increase collagen, proteoglycan, and other protein content to the ligament matrix. This process takes place along with the individual's maturation holistically, responding to loading by adapting (e.g., tibial spine growth in response to ligament loading).

If the loading is excessive (zone of structural failure), and injury occurs, the remodeling of ligament is more like scar tissue [64, 65]. Ligaments that have healed from injury may contain smaller, flawed, and less organized collagen fibers with a higher concentration of type III fibers and larger proteoglycan molecules [64, 66]. In addition, remodeled (compared with uninjured native) ligaments stretch more while under a low load over a long duration of time (i.e., "creep"), creating increased joint laxity. Theoretically, we could study how to optimize the strength of native ligaments within the knee; however, typically clinicians are interested in how to rehabilitate torn and reconstructed ligaments within the knee (i.e., cruciate and/or collateral ligaments, or some combination).

Following injury (or surgery), the healing ligament is affected by joint motion: decreased motion may prevent further tissue damage and resultant pain and swelling, though immobilizing a joint while the ligament heals can have negative outcomes (i.e., decreased ligament mass, stiffness, and strength) [67]. Decreased loading of the ligament also affects the structure of the ligament-bone junction (enthesis) causing the subperiosteal osteoclasts to resorb much of the ligamentous insertions on the bone [68]. Further, with immobilization the cross-sectional area of the ACL is reduced, hypothesized to be due to a loss in collagen fibrils, glycosaminoglycans (GAGs), and altered remaining collagen fibril orientation [69]. In contrast, joint motion (active or passive range of motion [ROM]) and/or loading leads to more connective tissue (with a smaller percentage of cross-link pattern of collagen), increased localized blood flow, and increased ultimate strength of the ligament. Different ligaments may heal at different rates, and when a combination of ligaments are injured, they heal with inferior ligamentous quality and more slowly than with isolated injuries [69–76]. Following ligamentous surgical reconstruction, the reconstructed graft strength will eventually exhibit similar ultimate strength, but will vary depending on graft type, donor age, and donor characteristics (autograft vs allograft, patellar tendon vs hamstring graft) [77, 78].

2.2 Tendon Response to Loading

Tendons transmit tensile loads from the muscle to the bone and store and release mechanical energy that can be harnessed for joint motion [79]. Tendon cells, tenoblasts or tenocytes, are dispersed throughout collagen bundles and produce the components used to build the extracellular matrix, including collagen, fibronectin, and proteoglycans [80]. The hierarchical structure of the extracellular matrix is critical to the ability of tendons to withstand high tensile loads [81]. Additional cells, termed tendon stem cells, are present and contribute to tendon maintenance and repair [82].

Tendon responds to applied mechanical load by adapting characteristics including cross-sectional area, mechanical stiffness, microstructure, and blood flow. Again, via the aforementioned process of mechanotransduction, tissue loading results in a strain on the tendon cells, which then convert the mechanical stimuli (often compression or shear) into cellular responses that promote structural changes [54].

A primary load-induced response in the tendon is an upregulation of insulin-like growth factor-1, which is associated with cellular proliferation and matrix remodeling [83]. That is, the tenocytes detect loads from the extracellular matrix of the tendon and in turn modify the extracellular matrix in accordance with the load.

The initial response of the tendon to loading is an increase in collagen turnover followed by predominately anabolic processes resulting in an increased net synthesis of collagen [81]. For example, the collagen synthesis in the patellar tendon doubles within 24 h of exercise-related loading [84]. This pattern of degradation and formation with an overall net synthesis that is observed in the tendon is similar to what is seen in skeletal muscle in response to loading. This net synthesis of collagen leads to an increase in tendon cross-sectional area or stiffness [85]. Increased cross-linking of existing collagen fibrils has also been acutely observed following loading, [86, 87] which increases tendon stiffness without a corresponding increase in cross sectional area. [87]

Tendons are highly responsive to a variety of loading regimens, with strong evidence indicating that load magnitude has a primary role in tendon adaptation. Higher load magnitude results in greater strain, with a certain level of strain being necessary to induce tendon adaptation. For example, Achilles tendon stiffness increased in response to 14 weeks of plantar flexor training at strain levels of 4.5%, but not at strain levels of 3% despite equal loading frequencies and volumes [88]. A similar response is observed in the patellar tendon, where increased stiffness resulted from heavy resistance training (70% 1RM) but not light resistance training (~ 15% 1RM) of equal volume [89]. Thus, loading magnitude, more so than volume, appears to be a dominant factor in driving tendon adaptation.

Borrowing from bone mechanics, the "mechanostat" theory has been used to describe a tendon's response to load [90]. That is, a mechanical load or stimulus of a certain level (mechanostat point) maintains tendon homeostasis and potentially elicits positive adaptations [91]. When the load is above (overload) or below (underload) this level, maladaptive responses occur including increases in inflammatory cytokines, markers of apoptosis, and digestive enzymes, resulting in tendon weakening, reduced capacity for load, and increased potential for tendon pathology and pain [91]. Excessive loading of the tendon can also promote an increase in non-tenocyte differentiation of tendon stem cells, contributing to the development of tendinopathy [92].

Importantly, the mechanostat point shifts based on the nature of the long-term load to which the tendon is exposed. In a chronically under-loaded tendon, the mechanostat point will shift such that the under-loaded state becomes the new homeostatic state, creating a tendon with limited capacity for load tolerance. For example, a substantial decrease (~ 30%) in stiffness of the patellar tendon occurs within 3 weeks of unloading [93]. A deconditioned tendon will have limited tolerance for loads associated with activities that were once easily tolerated and commonplace. Conversely, chronic exposure to appropriate loading that elicits an adaptive response has been proposed to gradually shift the mechanostat point and increase load capacity [91]. Doing so results in a tendon that can now tolerate loads with activities that are more aggressive and that previously induced an overload maladaptive response. Exploiting this characteristic is at the core of successful athletic conditioning approaches and injury rehabilitation programs.

2.3 Meniscus Response to Loading

The complex material and structural properties of menisci must be described before understanding how they adapt to different forms of loading (including forms of exercise). Menisci have a fibrocartilaginous structure that is primarily made of collagen [94]. Roughly 70% of the dry weight of meniscus is collagen, and that is mostly (90%) type I collagen, with smaller amounts of type II, III, V, and VI collagen also present. The inner meniscal zone is less vascularized, more cartilaginous, and predominantly type II collagen, while the outer zone is more vascularized, more fibrous, and mostly type I collagen [31, 95, 96]. Further, type I collagen forms the mechanical ring structure of the meniscus, attaching to the tibial spines via the anterior and posterior horns. The ring structure of menisci is important for mechanical function (i.e., maintaining the loading through the meniscus, rather than entirely through the femoral and tibial articular cartilage), and the capacity for load distribution decreases when the ring is broken. In addition, to distribute a load across the joint, GAGs hold water within menisci, comprising only a small portion (2.5%) of the dry weight, but are responsible for load distribution within the collagen matrix [94]. The actual water content of menisci has been found to be approximately 75%, with about 2% more in the inner zone of menisci in comparison to the outer zone [97].

Glycosaminoglycans and water content within the menisci adapt to external loading. When the menisci are loaded, they can be "extruded" beyond the tibial plateau boundaries. Thirty minutes of running in trained marathoners resulted in decreased markers of GAG content within the anterior and posterior horns of the medial meniscus [98]. Athletes who participate in a much longer race than a marathon, such as the 2017 Gore-Tex® Transalpine run (over 270.5 km and 16,453 m of vertical distance), were monitored for medial meniscus extrusion over the race and then again at 2 weeks following the race [99]. Medial meniscus increasingly extruded over the race duration, but was not significantly different from baseline after 2 weeks of recovery following the race [99]. In a cadaveric model, changing

the fully extended knee from a valgus to a varus alignment, while under 750 N of axial loading, caused the medial meniscus to extrude medially and resulted in increased tibiofemoral peak contact pressure [100]. In a follow-up study, when the medial meniscus was incrementally resected to mimic meniscectomy, tibiofemoral contact pressure also increased [101]. Altered lateral compartment loading may also be present following a medial open-wedge tibial osteotomy, as progressive deterioration was found throughout the regions of the lateral meniscus on magnetic resonance imaging [102]. Cartilage on the tibial plateau is protected from strain by the menisci, even during walking, as after 20 min of walking, areas of the medial tibial cartilage that were not covered by the medial meniscus demonstrated increased strain in comparison to cartilage that was covered [103]. Glycosaminoglycans in the outer circumference of the meniscus increase tissue viscosity and stiffness, and in the middle and inner meniscus, GAGs increase loading capacity [104]. Loading has been shown to temporarily increase the production of GAGs [105, 106], even increasing the hydrostatic and osmotic pressures resulting in an increased ability to distribute load [107]. The impaired meniscal loading capacity in the knee of humans with osteoarthritis, with reduced loading capacity of articular cartilage, is thought to result in an increased (50% greater) GAG content in the outer circumference of the menisci when compared with menisci from a healthy knee [97]. Increased GAG content in the outer circumference of the meniscus, found in those with knee osteoarthritis, would lead to increased viscosity and stiffness of the knee [104].

Material and structural components of menisci are balanced with anabolic and catabolic physiology [56] through cells that have been called "fibrochondrocytes" [56]. Joint loading, along with genetic and biochemical factors within the joint (i.e., growth factors and cytokines) [108–110], play a role in balancing anabolic and catabolic activity. The structure and material property of menisci were found to be negatively affected in chickens exposed to strenuous treadmill running, causing a decrease in dermatan sulfate proteoglycans and pyridinoline crosslinks, but only in young runners [111]. This deceased crosslink formation was discussed as potentially negatively affecting the material properties of menisci; however, all material properties returned to normal and were not different when the chickens reached skeletal maturity [111].

In vivo, joint immobilization without loading has been found to negatively affect the material properties of menisci. Immobilization was found to lead to a gross decrease in proteoglycan content within menisci [112], and more specifically, at the gene expression level of aggrecan (the primary proteoglycan within menisci) [113]. Mobilization of the joint (i.e., immediate post-operative passive ROM, WB, and daily walks) was found to lead to better outcomes when compared with cast immobilization in a dog model following a medial meniscus lesion [114], and in a rabbit model compared with no loading [115].

Ultimately, loading affects the properties of menisci but we know very little about how to optimize load magnitude, type, and duration to encourage healing [116]. Immobilization is not supported by the evidence, but a period of time with partial WB following meniscal injury, repair, or partial meniscectomy has been found to result in improved outcomes [116]. Recently, the anabolic activity of collagen was studied over the lifetime of 25 human menisci, 18 with knee osteoarthritis and 7 without using 14C bomb pulse timing and results indicated that there was negligible turnover of collagen in any of the adult menisci [97]. The conclusion from these studies supports findings of meniscal degeneration in individuals including and beyond middle-age. Anabolic strengthening of menisci collagen structure through physical loading may not be possible in adults and is currently unknown in childhood [97]. There is speculation that a physically active lifestyle in childhood and teenage years has potential to positively affect meniscal collagen content and material structure [117], but this is as yet unstudied.

2.4 Articular Cartilage Response to Loading

Articular cartilage responds to mechanical stimuli via altered cell metabolism and matrix synthesis [118]. The absence of normal knee loading and movement may induce cartilage thinning and degradation [119]. In vitro and animal studies have demonstrated the effect of frequency, rate, and amplitude of tissue loading on cell activity and cartilage tissue recovery, with dynamic, cyclic and shear loading generally exhibiting a positive effect, while static loading (as well as unloading or low-frequency loading) is more catabolic in nature [120–142]. Canine studies have shown increases in cartilage thickness with running [143–146]. Within human (and sporting) studies, the acute (and recovery) cartilage response to different rehabilitation exercises and sporting and recreational activities such as walking, cycling, and running, as well as the type, duration and/or intensity of these activities have been explored [6, 98, 147–155].

Eckstein et al. demonstrated a 6% and 5% reduction in patella cartilage volume after 50 [6] and 100 [155] knee bends, respectively, with 90 min of non-WB (NWB) required to restore pre-activity cartilage volume [155]. Another study demonstrated a mean reduction of 4.7% in patellar cartilage volume after a 90° sustained squat for 20 s, vs a 5.9% reduction following a repetitive series of 30 squats through 120° of knee flexion [156]. This is likely due to the larger surface area involved in dynamic exercises [156], combined with the variation in duration (time required to complete the tasks) and repetition of the two different tasks. Tibiofemoral cartilage deformation has been investigated following

activities including 30 unilateral knee bends, a 2-min unilateral stance (with 200% of body weight), and 10 jumps from a 40-cm height chair on to one leg [148]. While no change was observed in the femoral condyles after the jumps, a significant reduction was observed in the medial (mean 6.1%) and lateral (mean 7.2%) tibial cartilage, though changes were not significant during the other tasks. The varied deformation attributed to different tasks such as those outlined above highlights the importance of considering a range of loading variables (and the potential interaction of these) when prescribing exercises to healthy and pathological populations, including the duration, magnitude, frequency, and rate of loading. A trend toward less cartilage deformation has also been observed in trained (vs untrained) individuals [148], although the role of the training level on the cartilage deformational behavior requires further investigation. Interestingly, joint movement in the absence of loading appears unable to restore atrophic cartilage changes [157], suggesting mechanical forces are more important than motion in supporting normal cartilage properties [158]. Nonetheless, studies have demonstrated the potential for continuous passive motion to enhance cell processes, tissue quality, and histological content after chondral injury [159–163], and may also benefit cartilage and joint health during rehabilitation via the metabolism of lubricin, a chondroprotective molecule found in synovial fluid and the cartilage surface [164].

Mean patella cartilage deformation after different types of exercise has been investigated, including 2.8% after walking (for 5 min), 5.0% after running (for 200 m), and 4.5% after cycling (10 min at a frequency of 80 Hz) [148]. These activities all vary in the components of loading including the magnitude and rate of loading, as well as the frequency and duration of loading. In a study of active triathletes and inactive controls, the active group displayed a greater total surface area of the tibial and patella cartilage, albeit no differences were observed in cartilage thickness. The increased surface area may suggest an adaptation of the cartilage tissue to greater and repetitive loads, thereby acting to preserve (rather than increase) normal cartilage thickness [165]. In patients following medial meniscectomy and at risk of developing knee osteoarthritis, a positive effect on knee cartilage GAG content resulted from moderate exercise [106]. Racunica et al. [166] reported that vigorous physical activity increased tibial cartilage volume and was inversely related to the presence of cartilage defects, with studies also demonstrating no adverse cartilage changes in the short term [167, 168] and long term [169] after marathon running. However, Stehling et al. [170] demonstrated that asymptomatic middle-aged subjects classified into a 'high-activity' group (vs 'low- or moderate activity') demonstrated an increasing incidence of cartilage defects, bone marrow edema, and joint effusion. In a study of patients with knee osteoarthritis risk factors and normal control subjects, categorized based on activity level and self-reported frequency of knee-bending activities, those at risk of knee osteoarthritis participating in more strenuous exercise and more frequent knee-bending activities demonstrated changes suggesting greater cartilage degeneration [171].

While moderate mechanical loading of the joint aims to maintain the integrity of articular cartilage [172], joint disuse or overuse may result in cartilage degradation [172–174]. Both acute and chronic high-intensity loads cause cartilage degeneration [175], and excessive loading may promote a relative imbalance between anabolic and catabolic activity resulting in the depletion of important extracellular matrix components [176, 177]. Reduced knee joint cartilage thickness has been observed with forced immobilization or a period of partial WB [178, 179]. Animal and in vitro studies have highlighted the loss of proteoglycans, cartilage thinning/atrophy and softening, as well as other negative changes that occur with joint unloading/immobilization [157, 173, 174, 180–186]. It is also possible that extended periods of unloading/immobilization may promote biochemical and biomechanical changes in the longer term that may limit the tissue's ability to respond appropriately to mechanical loads [182, 187].

2.5 Bone Response to Loading

The ongoing remodeling process inherent in bone seeks to regulate bone microstructure as well as overall geometry in response to the changing mechanical environment [188], and it is the cells that govern the process of turning the physical forces experienced into biochemical signals that regulate the bone adaptive and regenerative process. Mechanical stimulation of osteoblasts and osteocytes activates pathways that subsequently stimulate the production of anabolic growth factors and the synthesis of matrix mineral and proteins [189, 190]. The adaptive process of bone mass to different mechanical loading conditions has been well reported [191–196]. Physical activity can enhance bone mineral density, with active individuals demonstrating greater density values [197–201]. Impact (and WB) activities and sports have been shown to increase bone mineral density, with NWB activities not having the same effect [202–208]. The response of bone to repetitive loading has been reported, with cortical thickness significantly greater in the dominant (vs non-dominant) arm of professional tennis players [209]. Immobilization and weightlessness can reduce bone mineral density [199, 210, 211].

In the knee joint, the subchondral bone, inclusive of both the subchondral bone plate and subchondral trabecular bone [212], is intimately associated with the articular cartilage [213]. The subchondral bone acts as the mechanical joint support linking to the diaphyseal bone [214], and provides a stress-absorbing function and supports

the metabolism of healthy joints [215]. In addition to its shock-absorbing capabilities, the subchondral trabecular bone may also be important for supplying nutrition to the articular cartilage [216]. Separating the deeper layers of the articular cartilage and the subchondral bone is the osteochondral junction [214], consisting of the deeper non-calcified cartilage, the tidemark, a calcified layer of cartilage and the subchondral bone plate [217]. The calcified cartilage layer is permeable and is important in the biochemical interaction between the deeper non-calcified cartilage layer and the underlying subchondral bone [218]. A range of factors may affect the integrity of the subchondral bone, including genetic predisposition, sex, age, obesity, joint malalignment and geometry, previous history of joint injury, and physical activity [215].

With respect to physical activity and exercise, the specific effects on the subchondral bone may vary based on the mode, rate, intensity, and duration of the activity [219]. Animal studies have reported enhanced subchondral bone remodeling with a thicker subchondral bone plate and higher trabecular volume with running [220]. In humans, Wilks et al. [221] reported that tibial bone strength indicators appeared related to exercise-specific peak forces, with cortical bone density inversely related to running intensity. They proposed that musculoskeletal forces related to running can induce enhanced bone strength via adaptation, with these changes greater in sprinters, followed by middle-distance and long-distance runners, walkers, and then control subjects [221]. However, overloading may induce bony microdamage [222], in the form of both diffuse microdamage and microcracks [223], and it is this early damage that contributes to the initiation and progression of osteoarthritis [224]. Given the subchondral bone thickening that has been reported in the presence of osteoarthritic changes, the increased bone mass and stiffening may reduce its capacity as a shock absorber for the cartilage [225, 226]. Furthermore, bone marrow lesions may represent increased bone turnover [227] and may be reflective of increased compartmental knee loading [228]. In the presence of ongoing abnormal mechanical loading, subchondral microfractures are observed and bone marrow lesions persist and, while the amount of bone may increase as part of this process, the bony structure is affected via reduced mineral density [214, 229]. While bone marrow lesions are associated with pain and the progression of osteoarthritis [227], they can also be observed in people at risk of developing osteoarthritis before symptoms are experienced [230]. A systematic review reported that increased knee compartmental loads (and body mass) resulted in an increased presence and progression of bone marrow lesions, though contradictory findings for the association of bone marrow lesions and physical activity were reported [231]. This may in part be due to a dose–response relationship, and that the effect of physical activity may vary depending on the context (such as the presence of structural lesions and/or joint malalignment) in which it is performed [231].

3 Knee Rehabilitation, Training Principles and Loading Considerations

Following injury (or surgery) to structures around the knee, the primary goal of rehabilitation is to maximize the patient's response to exercise at the current level of function, while minimizing the risk of re-injury to the healing tissue [232]. In this respect, practitioners aim to improve the athlete's load capacity, both in terms of local-tissue and sport-specific capacity. We define local-tissue capacity as a specific structure's ability to withstand tissue-specific cumulative load. Sport-specific capacity is defined as the athlete's ability to perform (and withstand) the demands of training and competition [43].The balance between load and load capacity is thought to play a significant role in injury causation [233]. When the load that is applied to a tissue greatly exceeds that tissue's capacity, injury risk is increased. Complicating the load-capacity issue, is that for a tissue to adapt and load capacity to increase, gradual progressions in load that are *slightly greater* than current tissue capacity, are required. Therefore, for improvements in load capacity to occur, load must be increased, but not so much as to injure the tissue (and ultimately decrease load capacity) [44]. A final, and often neglected part of the load-capacity puzzle is consideration of the athlete's health. The load that an athlete can tolerate today could be quite different to tomorrow, simply due to decreases (or increases) in health [234].

3.1 The Workload-Injury Model: The Positive and Negative Effects of Training

The workload-injury model [235] draws upon the early work of Banister et al. [236], who first described the positive ("fitness") and negative ("fatigue") responses to training. Acute training load represents the short-term "fatigue" that arises from training, while chronic training load is analogous to "fitness" [49, 235]. Injury occurs when load exceeds the ability of the tissue to adapt (i.e., when load is greater than load capacity). Short-term training load (anywhere from one session to one week) is typically termed *acute training load,* while longer term training load is termed *chronic training load*. For many years, it was believed that injuries occurred as a result of high training loads. However, a recent review demonstrated that high chronic training loads are associated with a lower injury risk, while rapid increases in acute training loads increase risk [49]. These findings have been confirmed across multiple sports and research groups [237]. Of equal interest is the influence of high chronic load on performance. In the mid-1990s, Foster et al. [238] studied

the performance of runners, cyclists, and speed skaters and demonstrated that performance was closely linked to training load; athletes with higher training loads had faster time-trial performances. It appears that appropriately prescribed high chronic training loads reduce injury risk and enhance athlete performance in several ways. First, exposure to load helps athletes withstand subsequent load. Second, appropriately prescribed training develops physical qualities that not only protect against injury but allow athletes to perform the high-intensity tasks required of competition [239].

3.2 Load Monitoring and Tools for Load Monitoring

External load refers to the "work" completed during physical tasks. For example, the distance covered in different locomotor activities (e.g., walking, jogging, and running), the number (and intensity) of jumps, and the weight lifted during resistance training sessions are all examples of external load. Global positioning systems are commonly used to capture the locomotor activities performed by athletes. Some commercially available wearable technologies also incorporate additional inertial measurement sensors (i.e., accelerometers, gyroscopes, and magnetometers) that, when combined with customized algorithms, can detect sport-specific movements (e.g., jumping, tackling, diving) [240].

Internal load refers to the athletes' physiological, psychological, or biomechanical response to an external load [241, 242] and may include measures such as heart rate, session rating of perceived exertion (s-RPE) [238], perceived tissue damage (i.e., soreness), and even joint and muscle loads [242]. The internal load drives adaptation, whereas external load is used to manipulate the internal response [243]. In many cases (e.g., adolescent, amateur, and student athletes), capturing external load is problematic. For example, the technology used to capture external load (e.g., running, jumping, and cutting movements) is relatively expensive for most athletes. It is also difficult (not to mention impractical) to capture the external load of every single loading activity performed from early-stage rehabilitation through to return to performance. In many cases, practitioners often simply capture the internal load of athletes using s-RPE.

First described by Foster et al. [238], the s-RPE requires players to provide a subjective estimate of intensity using a 0 (rest) to 10 (maximal effort) scale. This intensity score is multiplied by the duration of practice or competition to provide "acute training load" for that session. "Training monotony" and "training strain" can also be calculated to provide an indication of the amount of variation within a training week. The higher the training monotony and training strain scores, the less variation (and likely recovery) within the training week. High training monotony may predispose tissues to overload. Training load represents a function of frequency, volume, and intensity. As such, increases or decreases of load can be made by manipulating frequency, volume, and/or intensity. The s-RPE allows clinicians to quantify internal load with minimal resources. Differential ratings of perceived exertion (d-RPE) have also been developed to describe the specific perceptual responses (breathlessness, leg muscle exertion, upper-body muscle exertion, and cognitive/technical demands) associated with training [244]. Despite the potential for s-RPE to quantify global internal training loads, it is unclear whether it has the sensitivity to quantify local tissue loading [43]. Modifications to the RPE scale may be required to adequately capture the loading performed by specific tissues. While rehabilitation training is often prescribed based on external loads (sets and repetitions of a specific exercise), there can be an uncoupling of external and internal load when athletes experience pain and/or maladaptation. Monitoring joint reactivity to loading at the knee joint can prove useful to quantify local tissue loading.

Joint reactivity is the recurrence of impairments (pain and/or soreness, effusion, reduced ROM, decreased knee muscle strength) due to the knee joint's response to increases in mechanical load during rehabilitation. Patients may complain of joint pain or muscle soreness when they progress to a higher level of load or activity. Muscle soreness is an indicator that the exercise is progressively overloaded; conversely, joint pain or the presence or reemergence of joint effusion can result in muscle inhibition and joint deterioration, and can increase the number of treatment sessions needed to achieve rehabilitation goals [245]. To monitor the progression of loads at the knee, joint pain and swelling can be used as adverse indicators of accelerated progression or tissue overload. Joint effusion grading and soreness rules are reliable in symptom monitoring, and for exercise and activity progression [246, 247]. Effusion can be monitored by performing the modified stroke test prior to, during, and after treatment. Grading ranges from no effusion to effusion that fills the joint so much that it is not possible to move out with a sweep (3 +) [247]. An increase in effusion following treatment that does not return to baseline likely indicates that load progression was too aggressive. Furthermore, individuals should be able to demonstrate the ability to tolerate lower loading demands without pain or swelling before progressing to higher loads. Soreness rules are based on when symptoms occur and are important to avoid extended recovery periods [246]. If joint soreness is experienced early in the treatment session, the intensity of the next exercise session should be reduced to a lower level to avoid the recurrence of symptoms. If joint pain or joint swelling is experienced after exercising, but the symptoms resolve before the next rehabilitation visit or after the next warm-up, then the program should not be progressed but rather maintained at the same level and monitored for reoccurrence of symptoms. A patient should ideally be able to tolerate one to three sessions

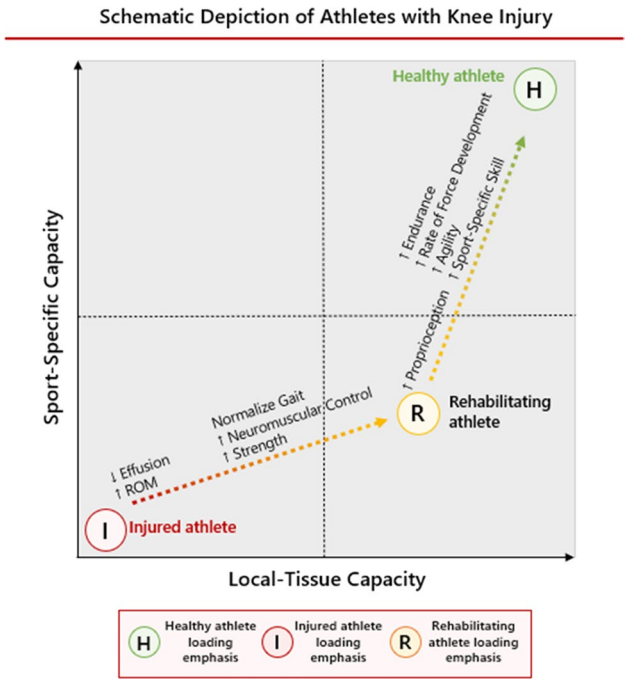

Fig. 5 The balance between sport-specific capacity and local tissue capacity for athletes with knee injury

at a specific intensity without any adverse responses before the intensity of the program is progressed [245].

3.3 Applying Training Load to Injury Rehabilitation

For optimal rehabilitation, clinicians should have a clear understanding of the specific injured tissue(s), and rehabilitation should be driven by scientific research of tissue-healing constraints, knee complex and lower extremity biomechanics, neuromuscular physiology, task-specific activities involving WB and NWB conditions, and training principles. Clinicians use movement as an intervention to produce physical stress to address body function, physical impairments, activity limitations, and participation restrictions [44]. This section focuses on applying principles of exercise prescription to optimize loading to tissues of the knee.

Identifying and achieving the appropriate/optimal mechanical loads to foster tissue healing presents challenges to the treating clinician. Tissue healing is influenced by the biology of the individual, such as age, sex, genetics, and tissue history (tissue type, previous injury, scar tissue, disease state) [248]. The loading environment can profoundly impact the nature, structure, and function of the healing tissue and wider neuromusculoskeletal system (rehabilitation environment, sports activity) [11]. Tissue healing is influenced by individual biology and the loading environment; tissues with a relatively higher capacity and tissue tolerance will heal faster than diseased and previously injured tissues with poorer capacity [11, 249]. Mechanical loading of the injured tissue through exercise needs to be dosed appropriately (i.e., type of load, magnitude, duration, frequency, rate, direction, intensity) in order to favorably influence cellular and neural adaptations [250]. Exercise dosage needs to be sufficient enough to produce these positive adaptations, but not excessive, which may result in re-injury or delayed tissue healing and recovery (Table 1). Recovery requires individualization of exercise based on joint reactivity (patient pain/soreness levels, swelling/effusion, impairments [reduced ROM or strength]), activity performance, and altered movement patterns.

By modifying the mechanical load elements, clinicians can alter the tissue adaptations, facilitate motor learning, and resolve corresponding physical impairments (Fig. 5). Providing different loads that create variable tensile, compressive, and shear deformation on the tissue through mechanotransduction and specificity can promote the appropriate extracellular synthesis. Even small variations in specific variable loading can protect tissue from abusive loads (peak loads, frequent loads) [50, 250]. As local tissue capacity is reestablished through manipulation of the different elements of load via tissue healing and impairment restoration (ROM, strength, balance, proprioception/neuromuscular control), sport-specific activities can be incorporated to further enhance local tissue capacity and provide the physical qualities required to tolerate the demands of the sports activity (Fig. 5) [43, 251, 252].

3.4 Key Principles of Training Load Management during the Rehabilitation Process

Historically, early management of knee injuries often included complete immobilization, but this has been shown to lead to weaker ligament healing and poorer outcomes [253]. Furthermore, immobilization resulted in reduction in articular cartilage thickness and mechanical stiffness [186, 254]. Current management advocates for a limited period of immobilization and promoting optimal loading, while protecting the healing tissues [255]. Clinicians can use mechanotherapy and load monitoring to design a safe exercise rehabilitation program. By using a systematic and personalized approach based on mechanical loading, tissue irritability and clinical milestones of impairments, clinicians can optimize the rehabilitation process to promote tissue healing and tissue resilience to enhance functional capacity. First, clinicians should apply the principles of exercise training program design (individuality, specificity, progressive overload, adaptation, progression, recovery, and reversibility) [256]. The balance between local tissue capacity and sport-specific capacity (Fig. 5) and information from Table 1 that we discussed earlier can be used to specifically target the tissue based on the nature of the load (mechanical

stimulus), and provide appropriate progressive overload to facilitate tissue repair and remodeling (Fig. 3).

The training process involves repetition of exercises designed for automatic execution of a motor skill and the development of structural and metabolic functions that lead to increased physical performance, and an increased ability to sustain the highest power output or speed of movement for a given distance or time (Fig. 4D). Return to sports participation represents an important societal/International Classification of Functioning, Disability, and Health indicator of a positive outcome, perhaps linked to improved levels of physical and mental health.

Clinicians should consider the minimum and maximum loads of safety. Using the physical stress to tissue and the envelope of function models (Fig. 3), minimum training loads should be established to ensure adequate loading is achieved and maximum training loads should be identified to reduce injury risk. Initial loads to the knee and changes in load should be individualized and targeted to the specific tissues to ensure an appropriate stimulus is provided.

Clinicians should use periodization principles and changes in training load should be in small, in line with the reduced tissue capacity [257]. Reiman and Lorenz [258] have provided a comprehensive clinical commentary on integrating strength and conditioning principles into the rehabilitation process. The current review expands on those principles as they apply to a knee loading program.

3.5 Prescribing Exercise Rehabilitation Loading Progressions to Ligaments

Ligamentous material and structural properties (as well as the selected graft type in the setting of post-surgical ligamentous reconstruction) should be a consideration for the rehabilitation specialist. In addition, descriptions of ligaments' response to exercise focus predominantly on the ACL, the medial collateral ligament (MCL) and posterior cruciate ligament (PCL), and less on the lateral collateral ligament (LCL).

Various models (direct measurement, in vivo, simulation) have been used to quantify the strain or tensile force during exercises, functional activities, and mobility to characterize knee ligaments that may be of help with exercise prescription [259–284]. Utilizing these measurements, exercise specialists can progressively load the ligamentous tissues with smaller strain and tensile forces during exercise in early phases of rehabilitation, when the ligament or reconstructed graft is healing, before progressing to later phases that include greater strain and tension.

The ACL provides 86% of the total resistance to anterior translation of the tibia relative to the femur [285]. When

Table 2 ACL loading (peak ACL force) based on activity and knee flexion angle

Activity	Knee flexion angle (°)	Peak ACL force (N)
ACL, peak load to failure [307]		2160
Weight bearing		
Barbell squat [278, 279]		0
Leg press [278, 279]		0
Forward lunge (both with and without a stride, using 12-repetition maximum load and through 90° of knee flexion) [280, 316]		0
Side lunge (both with and without a stride, using 12-repetition maximum load and through 90° of knee flexion) [316]		0
Dynamic squat to stand [288]	25°	20
Single-leg squat [289]	< 50°	~ 100
Double foot drop landing (stepping off a 60-cm platform) [291]	30°–50°	250
Level ground walking [317]	15°–20°	303
Single-leg landing from running to a stop [295]	25°–30°	1294
Non-weight bearing		
Dynamic seated knee extension (using 12-repetition maximum load and through 90° of knee flexion) [278]	15°	158
Isokinetic knee extension (0°–90° of knee flexion) at 180°/s [289]	35°–40°	254
Isokinetic knee extension (0°–90° of knee flexion) at 120°/s [289]	35°–40°	325
Isokinetic knee extension (0°–90° of knee flexion) at 60°/s [289]	35°–40°	349
Isometric seated knee extension [289]	35°–40°	396
Isometric or isokinetic knee flexion [289]		0

°/*s* degrees/second, *ACL* anterior cruciate ligament, *N* Newton

Table 3 ACL loading (peak ACL strain) based on activity and knee flexion angle

Activity	Knee flexion angle (°)	Peak ACL strain (%)
ACL, peak load to failure [299]		15.3
Weight bearing		
Riding a stationary cycle (75, 125, and 175 W) at both 60 and 90 RPM [270]	40°	1.2–2.1
Single-leg sit to stand, step up, step down, and forward lunge (1 × BW) [276]	30°	< 3.0
Squatting (1 × BW) through 90° of knee flexion [262]	10°	3.6–4.0
Simulated single-leg landing during deceleration [295]	25°–30°	2.5
Single-leg squat through 90° of knee flexion [290]	15°–20°	3.2
Walking gait at mid-stance [296]	−2° ± 8°	5 ± 4[a]
Walking gait at heel strike [296]	−4° ± 10°	12 ± 5[a]
Non-weight bearing		
100-N Lachman test [271]	30°	3
150-N Lachman test [271]	30°	3.5
Isometric seated knee extension using 27 N m of torque resistance [297]	30°	3.2
Dynamic seated knee extension with 45-N resistance [261]	0–90°	3.8
Isometric seated knee extension using 30-N m torque resistance [261]	15°	4.4
Isometric seated knee extension using 30-N m torque resistance [261]	30°	2
Isometric seated knee extension using 30-N m torque resistance [261]	60°	0.2
Isometric seated knee extension using 30-N m torque resistance [261]	90°	−0.5

ACL anterior cruciate ligament, *BW* body weight, *MRI* magnetic resonance imaging, *N* Newton, *N m* Newton meter, *RPM* revolutions per minute, *W* Watts

[a]These data were measured by MRI and high-speed biplanar radiography

the knee is between 0° and 60° of flexion, the contracted quadriceps creates force across the patellar tendon to create an anterior force on the proximal tibia, loading the ACL [285, 286]. However, the contracting quadriceps create posteriorly directed forces, in knee flexion angles greater than 60°, acting to unload the ACL [285, 286]. In contrast, the hamstrings create a posteriorly directed force throughout the entire knee flexion ROM, though increasing as knee flexion increases. When anteriorly directed quadriceps forces exceed posteriorly directed hamstring forces, the ACL experiences load and strain [259].

Loads across and strain on the ACL are smaller between 50° and 100°, in comparison to 0°–50° of knee flexion, and WB exercises generally load the ACL less than NWB exercises [259, 287]. Peak ACL force ranges from 0 to 300 N during WB activities with low knee flexion angles (Table 2) [282, 288–294]. However, a single-leg landing from running to a stop produces approximately 1300 N at knee flexion angles between 25° and 30° [295]. During NWB activities, ACL loads peak at 396 N but that may be dependent on the external load to the knee joint [278, 289].

Average peak ACL strain ranged from 1.2% (175 W and 90 RPM) to 2.1% (125 W and 60 RPM) across a range of power and cadence combinations, and occurred at a knee flexion angle of about 40° [270] (Table 3). Movements like a single-leg sit to stand, step-up, step-down, and forward lunge (without resistance) were found to have peak ACL strain of less than 3.0% and occur at 30° of knee flexion [276]. Strain values of 3.6–4.0% were found for squatting (through 90° of flexion) and occurred at 10° of knee flexion [262], and for a single-leg squat to be 3.2% and occurred between 15° and 20° of knee flexion [290]. As a reference, the 100 N (22.5 lb) and 150 N (34 lb) Lachman tests produced 3.0% and 3.5% strain, respectively, at a 30° knee flexion angle [270]. Using magnetic resonance imaging and biplanar radiography modeling of healthy subjects walking at 1 m/s, ACL strain at small knee flexion angles was 5% strain at midstance and 12% at heel strike [296].

NWB exercises such as the isometric seated knee extension using 27 N m of torque resistance (30° of knee flexion) was found to produce 3.2% ACL strain [297]. The dynamic seated knee extension with a 45-N (10-lb) resistance through a range of 90° of knee flexion was found to produce 3.2% ACL strain, and the isometric seated knee extension using a 30-N m torque produced 4.4%, 2.0, −0.2%, and −0.5% strain at 15°, 30°, 60°, and 90° of knee flexion, respectively [261].

Therefore, peak ACL loading during walking is similar to that measured while performing NWB seated isokinetic and isometric knee extension exercises and several times greater than WB exercises. Normalization of knee motion during walking is a common focus of rehabilitation following ACL reconstruction once pain, joint effusion, and symmetrical

knee extension are controlled [298]. Anterior cruciate ligament strain to failure using a mechanical simulation found that peak strain to failure was 15.3%; [299] therefore, exercise specialists do not approach these values with therapeutic exercises or functional activities commonly used during rehabilitation.

Both WB and NWB exercises and activities can and should be used after ACL injury and reconstruction (Tables 2, 3). However, there is evidence that those who perform predominantly WB exercises tend to have less knee pain, more knee stability, are more satisfied with results, and return to sport sooner [300]. Earlier introduction of NWB exercises (4 weeks following ACL reconstruction vs 12 weeks) may increase anterior knee laxity, but do not result in any difference in knee strength [300]. Even in the NWB seated knee extension exercise, patients did not progress to terminal knee extension ROM until the fifth week [300]. In contrast, others have shown that by adding NWB exercises between weeks 5 and 8 post-operatively, participants were not different in knee laxity to those who only performed WB exercises and were significantly stronger during isokinetic knee extension [301].

In the first few months post-ACL reconstruction, the ACL graft and the graft fixation sites are potentially much weaker than their eventual ultimate strength, achieved 9–12 months following ACL reconstruction, and therefore may be injured with less force. The exact amount of that force is unknown [302–304]; however, some researchers have estimated failure force in a sheep model. These studies, all of which involved Achilles tendon grafts and semitendinous tendon grafts, described this force as less than 750 N at 0, 12, and 24 weeks after surgery and then 1250 N at 52 weeks [305, 306]. As a reference, in healthy adults, the ultimate strength of the native ACL is approximately 2000 N (450 lb) [307]. The ACL graft does not initially have the same ultimate strength as the native ACL, but undergoes a process called "ligamentization" which increases ultimate strength over a period of months to years [308].

There are modifications to therapeutic exercises that may allow exercise specialists to manage loading further. Performing a squat with increased hip and trunk flexion can reduce ACL loading [290, 309]. Trunk flexion to approximately 30° was found to decrease ACL tensile forces by up to 24% and ACL strain by 16%, while the hamstring force was found to increase by 35% [290], reiterating the hamstrings' ability to resist anterior translation of the tibia on the femur. Squatting while maintaining the heels on the ground was found to have reduced ACL loading compared to squatting with the heels off the ground, perhaps related to the greater anterior translation of the knee and increased knee flexion in the latter task [289]. Maintaining the knees behind the toes in either a single-leg or double-leg squat will reduce ACL load, when compared to letting the knee go forward beyond the toes [278, 282]. Therefore, avoiding a vertically aligned trunk position, keeping the knees behind the toes, and keeping the heels on the ground are suggested to reduce ACL loading.

Managing the external load during NWB exercises (e.g., moving the external force proximally during a seated knee extension) may reduce ACL loading force, as is appropriate in the first few months following reconstruction [310]. When the goal is to minimize ACL loading, during seated knee extension exercises, this exercise should be performed at knee flexion angles between 50° and 100° and with the external resistance pad positioned proximally on the tibia (e.g., < 10 cm from the knee joint), particularly at knee flexion angles less than 50° (Table 2). Trunk flexion while performing a seated knee extension can be achieved by putting a wedge behind the person's back, while also placing the hamstrings at an advantage to unload the ACL.

Table 4 PCL tissue loading (peak PCL force) based on activity and knee flexion angle

Activity	Knee flexion angle (°)	Peak PCL force (N)
PCL, peak strain to failure [78, 401, 402]		739–4000
Weight bearing		
Squat and leg press (using 12-repetition maximum loading, and through 90° of knee flexion) [278, 279]	60°–90°	1500–2000
Level ground walking during loading response [317]	15°–20°	160
Non-weight bearing		
Isokinetic seated knee extension at (through 90° of knee flexion) at 180°/s [289]	90°	55
Isokinetic seated knee extension at (through 90° of knee flexion) at 60°/s [289]	90°	74
Isokinetic seated knee flexion (through 90° of knee flexion) at 180°/s [289]	90°	1952
Isokinetic seated knee flexion (through 90° of knee flexion) at 60°/s [289]	90°	2701
Seated isometric knee flexion [289]	90°	3300

°/*s* degree per second, *N* Newton, *PCL* posterior cruciate ligament

Table 5 Collateral ligament tissue loading (peak collateral strain) based on activity and knee flexion angle

Activity	Knee flexion angle (°)	Peak collateral strain (%)
MCL, peak strain to failure [299, 307, 321, 403]		17.1 (799 N)
MCL [323]	0°	0
MCL [323]	45°	1–2
MCL [323]	90°	2
MCL valgus knee testing using 25-N load at the ankle [322]	0°	2
MCL valgus knee testing using 25-N load at the ankle [322]	45°	4
MCL valgus knee testing using 25-N load at the ankle [322]	90°	5
MCL varus knee testing using 25-N load at the ankle [322]	0°	−1
MCL varus knee testing using 25-N load at the ankle [322]	45°	−1
MCL varus knee testing using 25-N load at the ankle [322]	90°	2
LCL, peak strain to failure [321]		(392 N)
LCL [323]	0°	0
LCL [323]	45°	0
LCL [323]	90°	−3 to −4
LCL valgus knee testing using 25-N load at the ankle [322]	0°	−2
LCL valgus knee testing using 25-N load at the ankle [322]	45°	−3
LCL valgus knee testing using 25-N load at the ankle [322]	90°	−3
LCL varus knee testing using 25-N load at the ankle [322]	0°	1.6
LCL varus knee testing using 25-N load at the ankle [322]	45°	3
LCL varus knee testing using 25-N load at the ankle [322]	90°	3

LCL lateral collateral ligament, *MCL* medial collateral ligament, *N* Newton

Graft type (autograft or allograft, and fixation) may help to determine loading in the first 8–12 weeks following ACL reconstruction, as soft tissue tendon (e.g., hamstring grafts) does not have the same fixation capacity as grafts with bones already on the ends (e.g., bone-patellar tendon-bone). Minimizing tensile loading on the hamstring graft during the first 4 weeks after reconstruction is especially important, to allow for soft tissue-bone interface strength, even up to 8–12 weeks following reconstruction [311, 312]. Fixation strength of bone autograft (i.e., patellar tendon graft) has been found to be achieved in 6–8 weeks [313, 314]. Further, the fixation and maturation of allografts are delayed in comparison to autografts (up to twice as long) [315]. Rehabilitation of an individual with a combined ligamentous injury (i.e., ACL and MCL), should consider using less resistance than in an individual with an isolated ligamentous injury.

Peak PCL forces generally occur near 90° of knee flexion, the bottom of the squat or knee flexion exercise, and may exceed four times the body weight (while the ACL is unloaded) (Table 4) [289]. Maximum PCL forces were found to be between 1500 and 2000 N during both squat and leg press (using 12 rep maximum loading, and through 90° of knee flexion), and to occur between 60° and 90° of knee flexion [278, 280, 282, 316]. For the knee extension exercise, PCL forces were found to be between 800 and 1000 N, and about 80° of knee flexion [278]. Reported values of PCL forces exceed 3300 N while performing a seated isometric knee flexion exercise at 90° of knee flexion [289]. The PCL is loaded approximately 160 N during walking on level ground and occurs at 15–20° of knee flexion during a loading response [317].

Peak strain to failure for collateral ligaments was found to be 17.1% [299, 318–320] (Table 5). Given the MCL resting length of 100 mm and the LCL resting length of 60 mm [321], the required forces for failure on the MCL and LCL would be 799 N and 392 N, respectively [321]. Collateral strain is close to 0% near full knee extension. During unloaded knee flexion the MCL was strained 1% to 2% at 45°, and up to 2% in 90° of flexion. The LCL did not strain while unloaded, was 0% at 45°, and by 90° was between −3% and −4% (i.e., they were relaxed). This suggests that the MCL lengthens with knee flexion, while the LCL is most taut in full knee extension. Furthermore, performing valgus testing by applying 25 N at the ankle created strains of 2%, 4%, and 5% in both directions for the MCL 0°, 45°, and 90° of knee flexion, respectively [322, 323]. While the MCL had a peak strain to failure of 5.1%, during a simulated drop landing in a cadaveric model, ACL loading was significantly greater at 15.3%, underscoring the greater risk of injury and failure to the ACL during athletic tasks such as drop landings [299].

Table 6 Patella tendon forces, stresses, and loading rates

Activity	Patella tendon force (×BW or N)	Loading rate (BW/s)	Patella tendon stress (MPa)
Bilateral leg press (3×BW or 1.5×BW per limb) [404]	5.2×BW	2.0	
Vertical jump (landing phase) [25]	5.17±0.86×BW	38.06±11.55	
Stop land/jump (horizontal landing phase) [405]	6.6±1.6×BW	93±23	
Decline squat at various board angles (0°, 10°, 25°) [406]	0°: 3479±1509 N at 77° knee flexion 10°: 4654±2104 N at 90° knee flexion 25°: 5683±2094 N at 105° knee flexion		
Forward step lunge behind the toes [407]			0.18
Forward step lunge in front of toes [407]			0.20

BW body weight, *MPa* Mega pascal, *N* Newton

3.6 Prescribing Exercise Loading Rehabilitation Progressions to the Tendon

Achieving a positive loading response in a pathological tendon is likely more challenging than in a healthy tendon, largely due to altered tissue structure and the presence of pain. The combination of these two factors compromises load capacity, eliciting a maladaptive response, which further negatively affects the tendon structure. At present, the ability of the degenerative portion of the pathological tendon to recover normal structure remains in doubt [324, 325]. It has been suggested that the disorganized architecture within the degenerative tendon region prevents a sufficient mechanotransductive response required to normalize the structure [326]. Conversely, the regions of the tendon surrounding the degenerative portion reveal greater amounts of aligned fibrillar structure that may provide a sufficient compensation for the tendon to tolerate load [326]. Thus, it has been proposed that a rehabilitation loading program can achieve adaptive benefits in the surrounding healthy tendon tissue, thereby enabling a successful clinical outcome [327]. The challenge lies in determining the acute and chronic training load parameters (magnitude, frequency, and duration) needed to adequately elicit the positive adaptive response without triggering the maladaptive responses associated with overload.

Early load management for a symptomatic tendinopathy should focus on reducing or eliminating high-intensity loads that provoke pain and structural disruption (Table 6). For an in-season athlete, this will most likely involve partial or full avoidance of sport participation. Adding a tendon-focused exercise program to the normal training demands can result in tendon overload and symptom exacerbation [328]. Incorporating loads that provide an immediate reduction in pain, such as sustained isometric contractions, should be encouraged to promote patient adherence to the loading program [329]. Immediate pain reduction was observed in those with patellar tendinopathy with either short-duration (10 s) or long-duration (40 s) isometric holds (85% maximal voluntary knee extensor contraction), when total time under tension was equal [330]. After 4 weeks of a loading program at ~80% maximum, patellar tendon pain reduction was similar whether isometric or isotonic loads were employed [331]. Similar to skeletal muscle, the activity and training history of the individual needs to be considered, as the same loading program used in athletes appears to be less effective in nonathletic or older populations [332].

In developing a successful loading program for tendinopathy, the following factors must be considered keeping in mind that a paucity of research exists comparing the various loading programs [333]. Loading intensity appears to be the primary factor in determining the extent of tendon adaptation, regardless of the contraction type (i.e., concentric or eccentric) [334]. During the early weeks of the loading program, reduced intensity may be beneficial to reduce the pain provoked by the exercises and promote patient adherence.

Successful outcomes have been observed when loading exercises have been performed twice daily or only three times per week [335–337]. This range of frequency is likely tied to the session volume (i.e., intensity and repetition) of the exercises, with higher session volume coupled with lower frequency. A 3-day recovery period between consecutive days of high-intensity loading has been suggested based on the tendon response to loading [338]. Loading programs for tendinopathy are recommended for a minimum of 12 weeks prior to considering other treatment options [335, 336, 338]. The loading program may need to be expanded beyond the minimum timeframe to optimize outcomes.

Eccentric loading is the frequent standard for tendinopathy rehabilitation, despite up to 45% of individuals not responding to the approach [339]. Exercise programs involving combined eccentric-concentric and isometric loading have demonstrated the same levels of effectiveness, indicating that the contraction type may be less important than other parameters of the loading program (e.g., loading magnitude, frequency, and duration) [333]. Avoiding

longer muscle–tendon lengths reduces the compressive loads created when the tendon wraps around the adjacent bony surface. As such, restricting joint ROM during loading exercises is commonly done for those with insertional tendinopathies and has also been suggested for use in those with non-insertional tendinopathies during the initial weeks of rehabilitation [338].

3.7 Prescribing Exercise Loading Rehabilitation Progressions to Meniscus

Reported loading progression and rehabilitation following meniscal injury varies widely [340]. Following injury, WB exercises should be performed as tolerated, and there is no clinical evidence to support limiting WB and/or knee ROM restrictions for improved healing [340]. Post-surgical failure rates are similar following meniscal repair on peripheral vertical meniscal tears when immediate post-operative WB is compared to protected WB regimens [341]. Concern is raised for use of the accelerated protocol when there is a radial tear, or even longitudinal tears greater than 3 cm. The reported timeline for progressing WB and knee ROM following meniscal injury ranges from 3 days after surgery, [342] to 4–6 weeks [343]. One important consideration is the age of the patient, as clinicians' expectations of the individual ability to increase knee extensor load after partial meniscectomy over the range studied (20–58 years) should decrease with increased age of the patient [344].

3.8 Prescribing Exercise Loading Rehabilitation Progressions to Cartilage and Bone

While the prescription of knee loading may be dictated by pain, symptoms, and the individual's response to loading, physiological loading is required to maintain the normal structure and function of both cartilage and subchondral bone [345, 346]. It is clear that even in the presence of acute injury, associated pain, and effusion, immobilization is detrimental to the structural integrity of both cartilage and bone [178, 179, 199, 210, 211], and also encourages knee joint stiffness and muscular atrophy. Tissue overload and overuse may also result in cartilage degradation and bony microdamage [172–177, 222], although defining 'overload' is not a simple task and may be relative to individual tissue properties, whether it is post-injury or in the early stages following a chondral repair or regenerative surgical procedure, such as microfracture, osteochondral autograft transfer system, and autologous chondrocyte implantation. Therefore, while it may be easier to identify and avoid joint immobilization and/or NWB, the presence of overload is relative to the specific environment and will also influence the recovery period required between loading bouts.

Irrespective of whether it is for a healthy individual, or one following injury and/or surgical intervention, when prescribing cartilage and bone loading progressions a number of factors require consideration, such as site loading, joint loading vs movement, physiological and anatomical factors, concomitant injuries, and post-operative factors. Site-specific differences (such as cartilage thickness and structure) are observed [347, 348], dictated by the loads (type, duration, frequency, and magnitude) more frequently encountered at specific locations. Therefore, an understanding of knee joint biomechanics will allow the clinician to modify the type of exercise (NWB or WB), degree of knee ROM, and the magnitude of external loading, in order to alter the loading environment relative to the patellofemoral or tibiofemoral joint.

Mechanical loads appear more important than joint motion in supporting normal cartilage physiological properties [158]. Furthermore, once atrophic changes are observed, joint movement in the absence of loading is unable to restore these changes [157]. More relevant to a post-injury or post-operative environment, while active or passive (such as continuous passive motion) movement may benefit cartilage and joint health, joint lubrication and limit stiffness [159–164], loading in some form should not be avoided.

A number of age-related cell and matrix changes occur within the cartilage [349, 350], effectively reducing its ability to respond adequately to mechanical loading [350, 351]. Both knee joint malalignment [352–354] and a higher body mass index [231, 355–361] are associated with greater compartmental knee loads and structural (adaptive and adverse) cartilage and bone changes. Furthermore, muscular weakness has an effect on reduced shock absorption and subsequent higher articular contact stresses [362], and quadriceps weakness in particular is associated with greater levels of knee joint loading during gait [363, 364]. Therefore, while mechanical loading is important, repetitive and chronic overload is detrimental, and these factors may require thoughtful consideration when prescribing exercise.

As already reported throughout this review, knee loading is influenced by a number of tissues, including the cartilage, meniscus, and ligamentous structures. Meniscal damage, chondral lesions, and traumatic ligamentous injuries may lead to (or be associated with) subchondral bone pathological changes [365–368]. Anterior cruciate ligament deficiency may alter knee kinematics [369], and could contribute to the degenerative changes observed in cruciate-deficient knees with loading during WB activities shifted toward areas that have not adapted to these loads [370]. A number of changes are also observed with osteoarthritis [371, 372], subsequently promoting a reduction in tissue stiffness [373, 374], with progression of the disease resulting in cartilage delamination and subchondral bone exposure [375]. Subchondral bone pathology may alter the

Table 7 Knee joint loading in various activities

Activity	Kinematics	Tibiofemoral compressive forces (% body weight)	Tibiofemoral shear forces (% body weight)	Tibiofemoral cartilage deformation/strain	Patellofemoral compressive forces (% body weight)	Patellofemoral shear forces (% body weight)	Patellofemoral cartilage deformation/strain
Aquatic weight bearing (water level) [408]		0.08×BW (C7) 0.15×BW (shoulders) 0.28–0.35×BW (Xiphisternal) 0.47–0.54×BW (pubic symphysis to umbilicus)					
Elliptical [409, 410]		0.9–2.5×BW	0.15×BW anterior shear		0.8–1.9×BW (7.9–19 N/kg)		
Anti-gravity treadmills (1.5–4.5 mph) [411]		25%: 0.8–1.9×BW 50%: 1.2–3.0×BW 75%: 1.5–3.7×BW 100%: 2.1–5.1×BW					
Two-legged stance		1.07×BW					
Stationary cycle [148, 409, 412]		1.2–1.8×BW (forward) 1.0×BW (backward)	2.1×BW anterior (forward) 2.8×BW anterior (backward)		1.2–1.7×BW (forward) 2.3×BW (backward)	0.7×BW (forward) 0.8×BW (backward)	4.5%/NA
Stepper/stair climber [409]		2.4–3.3×BW					
Kneeling [413, 414]		5–6.3×BW		7.1%/6.5%			7.8%/7.1%
Level walking [148, 409, 415–419]		1.5–3×BW		8%/NA	0.5–1.3×BW		2.8%/NA
Sitting down [420]		2.25×BW					
Standing up [420]		2.46×BW			2.8–5.5×BW		
Knee bending [148]		2.53×BW		6.5%/7.2%			7.1%/7.8%
One-legged stance		2.59×BW					
Stair ascending [420]		3.16–5.3×BW			2.1–3.3×BW		
Stair descending [420]		3.46–4.3×BW			5–5.7×BW		
Tennis [409]		4.2×BW serve 4.3×BW forehand 3.5×BW backhand	0.28×BW anterior shear				
Golf [409]		4.5×BW lead 3.0×BW trail	0.34×BW anterior shear				
Rowing [409, 421]		0.85–5.4×BW (intensity-dependent)					
Squatting [148, 278, 413, 422]		3–17.3×BW 20×BW (deep)		7.2%/7.2%	6.0–7.6×BW		4.7–8.2%/8.2%

biomechanical force distribution across the cartilage surface and/or disrupt the osteochondral junction [217, 226]. Bone marrow lesions are also associated with pain and the progression of osteoarthritis [227], and have been identified in a range of patient cohorts including, but not limited to, patients with osteoarthritis, those following acute ACL rupture, patients with meniscal pathology or traumatic and chronic chondral lesions, or those following cartilage procedures such as marrow stimulation or autologous chondrocyte implantation [215, 365–368, 376–379]. Therefore, consideration of concomitant pathology may affect the knee loading profile during rehabilitation and ambulatory activities.

When prescribing loading progressions in the earlier stages after knee surgery in general, a number of other factors may require consideration. For example, while the synovial fluid provides nutrition to the cartilage [380], its viscosity contributes to its load-bearing and lubrication capacity [381]. This fluid is drained at the time of knee surgery and may take some time to be appropriately restored [382]. The nature of the chondral injury and surgical procedure may also require consideration. If a chondral injury extends into the subchondral bone, bone marrow mesenchymal progenitor cells can flow into the defect, promoting a fibrocartilage repair [383], which is structurally and biomechanically inferior to hyaline cartilage. Furthermore, surgical cartilage repair techniques (such as marrow stimulation) seek to violate the tidemark and promote a fibrocartilage repair process, with reports suggesting that failure of microfracture may be expected beyond 5 years post-operatively [384]. Nonetheless, in vitro models of microfracture have demonstrated that controlled dynamic compressive loading enhances chondrogenesis, with generation of more hyaline-like cartilage and improved integration with the surrounding tissue [385]. Other surgical methods for regenerating hyaline-like cartilage such as autologous chondrocyte implantation have been employed, with the latter having been reported to be more effective than microfracture [386]. Regardless, the primitive hyaline-like or fibrocartilage repair that may be present early after injury or surgery is often a biomechanically inferior substitute that is unable to withstand the same mechanical demands as normal hyaline cartilage [387, 388].

With respect to knee cartilage loading and rehabilitation, an understanding of joint arthrokinematics is also important so that the clinician can manipulate the degree of WB, knee ROM, and exercise modality based on the location of the cartilage lesion. With knee flexion and extension there is a combined roll, glide, and spin of the articulating tibiofemoral surfaces [389, 390], which creates shear and compressive cartilage stress, whilst also altering the contact area and pressure. Subsequently, within the patellofemoral joint, the patella glides superiorly and inferiorly during flexion and extension, with the patella not making initial contact with the articulating trochlea until 20° of knee flexion (from full knee extension) [391], with the patellofemoral contact area increasing with further knee flexion. Therefore, with this in mind, joint loading using graded exercises should start with the introduction of activities that are less than body weight and combined with limited joint motion activities to facilitate healing and to reduce post-surgical complications (Table 7). Exercise equipment, such as stationary cycling or elliptical machines, can simulate low-load loading while WB and ROM restrictions are well maintained [392]. Patients can safely begin to incorporate joint loading exercises from 0° to 60° of knee flexion provided substantial compressive loads to the healing articular cartilage of the tibiofemoral joint do not occur. When full WB is indicated, graded resistive WB activities on land such as weight shifting, leg press, and mini-squats may be utilized. Current recommendations allow patients to begin a gradual return to more high-impact activities such as running, agility, and plyometric training after 16–20 weeks if the athlete demonstrates the ability to tolerate the demands of daily activities without adverse joint reactivity [245].

4 Conclusions

The knee joint is vulnerable to injury from mechanical loads during sporting activities. We have expanded on several models to clarify the understanding of how the structure-specific tissue responds and adapts to mechanical load and to better support the use of mechanical loads to facilitate appropriate exercise and activity selection and progression. A differential response to the various elements of mechanical loading occurs at the tissue structural and cellular levels of the ligaments, tendons, menisci, bone, and cartilage within and surrounding the knee. Through mechanotransduction, modifications that can occur at the cellular level facilitate extracellular matrix synthesis or degradation that then alter tissue mechanical and material properties, resulting in changes in structure-tissue capacity. Tools for monitoring rehabilitation training loads to the knee have been proposed to assess the reactivity of the knee joint to mechanical loading. Appropriate selection of exercises, functional activities, and mobility tasks based on their mechanical load profile can be utilized during rehabilitation to systematically and progressively load the structure of the knee to promote tissue healing and repair.

5 Glossary

Acute training load: The training performed over a short-term period. Acute training load can be as short as one training session, but usually corresponds to a 1-week time period or less. Acute training load is commonly used to reflect the "fatigue" that arises from training [49, 235].

Chronic training load: The training performed over a long period. Chronic training load usually corresponds

Table 7 (continued)

Activity	Kinematics	Tibiofemoral compressive forces (% body weight)	Tibiofemoral shear forces (% body weight)	Tibiofemoral cartilage deformation/strain	Patellofemoral compressive forces (% body weight)	Patellofemoral shear forces (% body weight)	Patellofemoral cartilage deformation/strain
Knee extension exercise [422, 423]		5.7–7.5 × BW (4598 N)	0.8–1.6 × BW anterior shear (1178 N)				
Leg press [422]		2.8–7.8 × BW (5762 N)	2.3 × BW (1667 N)				
Squat exercise [422]		8 × BW (6139 N)	2.4 × BW posterior shear (1783 N)		7.8 × BW		
Single-leg squat [424]	Knee 92–94°, 1.14–1.22 N m/kg						
Reverse lunge [424]	Knee 63–66°, 1.41–1.50 N m/kg						
Lunge [420, 424]	Knee 61–63°, 1.36–1.40 N m/kg	3–4 × BW					
Uphill walking [425, 426]		4.7–6.4 × BW (increases with incline)	0.36–0.46 × BW (increases with incline)		1.5–4.2 × BW		
Downhill walking [425, 426]		3.7–8 × BW	0–0.12 × BW (increases with incline)		1.5–7 × BW		
Kicking					7.6 × BW		
Jogging [409, 427]		3.1–4.2 × BW					
Running [419, 428, 429]		3–8 × BW		2–6%/NA	5.6–7.7 × BW		3–4%/NA
Hopping [420]		4.5–7 × BW			3.5–6 BW		NA/2%
Jumping (jump/land) [430]		6.9–9 × BW	0.3–1.4 × BW anterior shear 1.0–3.1 × BW posterior shear		20 × BW	2–2.4 × BW	
Drop jump [429, 431]		9.1–14.6 × BW		1–3%/NA			2–3%/NA

BW bodyweight, *N* Newton, *NA* not available, *N m* Newton meters

to a 4-week time period, although may range from 3 to 6 weeks. Chronic training load is commonly used to reflect the "fitness" that arises from training [49, 235].

External load: The "work" or exercise volume, intensity, and/or frequency completed during a physical task, such as distance covered in locomotor activities (e.g., walking, jogging, and running), the number (and intensity) of jumps or throws, the weight lifted during resistance training sessions, and acceleration/deceleration-based activities [393–397].

Fatigue: The sensations of tiredness and associated decrements in muscular performance and function [398]. Fatigue is the athlete's response to excessive or rapid changes in training load, and is influenced by the central nervous system, cardiovascular system, and musculoskeletal systems. It is generally transient, and is subjectively impacted by social, cultural, psychological, and environmental factors. Systemic illness should be excluded [399].

Fitness: A single attribute (or capacity), or set of attributes that people have or achieve that relates to the ability to perform physical activity [400].

Internal load: Refers to the athletes' physiological, psychological, or biomechanical response to an external load. [241, 242] These may include measures of heart rate, session-rating of perceived exertion [238], perceived tissue damage (i.e., soreness), blood lactate concentration, and even joint and muscle loads [242].

Mechanical loading: The physical forces that act on or create a demand on the body at the systems level, anatomical structures at the organ and tissue level, and ultimately to the molecular and cellular level [7]. Mechanical loading can be characterized by the magnitude, duration, frequency, rate of force development, and the nature and direction of force application.

Sport-specific capacity: The athlete's ability to perform (and withstand) the demands of training and competition [43].

Tissue load capacity: The ability of a musculoskeletal structure to withstand tissue-specific cumulative load [40]. This is dependent on the type and status of the specific tissue, which can vary between individuals.

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