

Review Article

Muscle Structural and Functional Adaptations and their Osteoarthritis Linkages: Clinical and Preclinical Observations and Tentative Hypotheses

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Abstract

Osteoarthritis, the most prevalent musculoskeletal disease affecting older adults remains an enormous public health challenge. A disease with multiple disabling physical manifestations including joint tissue damage, inflammation and stiffness, more clearly needs to be done to retard its progression and emergence wherever possible. Building on prior reviews capturing almost all data on this topic prior to 2020, here we present some newer data that elaborates on muscle as a key joint structure that may have a bearing on osteoarthritis joint damage and its progression. Most if not show this is a topic that can advance osteoarthritis understandings as well as its mitigation and should be pursued.

Keywords: Aging; Atrophy; Joint; Intervention; Muscle; Osteoarthritis; Sarcopenia; Weakness

Introduction

It is apparent that osteoarthritis, the most common joint disease and one which disables many older adults has been well researched for more than a century, but to no conclusive avail as to its origins that appear to be multifactorial and currently relatively unresponsive or impervious to the application of various intervention approaches. Often only diagnosed in its later disease stages, it is accepted that this disabling disease is irreversible and progressive [1]. Most commonly attributed to age and injury associated linkages there is however a limited or accepted universal understanding of the complex disease mechanisms of osteoarthritis and their temporal trajectories and why most palliative interventions fail, while others such as exercise appear somewhat efficacious [2,3].

The problem here may however stem from the limited conceptual model of the disease and its common characterization as a disease solely involving articular cartilage tissue and problems in extrapolating laboratory based studies that actively employ invasive or inflicted joint pathology in varied animal species to simulate those that emerge without any visible cause in the clinical realm. Additionally, in clinical studies, it is not possible to ensure 'control subjects' are indeed 'disease free' with comparable health status and gender distributions. Additionally, the use of multiple subjective measures, rather than singular objective muscle and kinetic oriented measures with well established measurement properties, plus a focus on local muscle attributes alone to the exclusion of other muscles and motion determinants, renders its cumulative interpretation highly challenging at best. Moreover, even though more recent acceptance of osteoarthritis as a disease encompassing all joint tissues, such as the joint capsule, joint ligaments, tendons and synovial membrane lining and that includes extensive focal as well as systemic mobility changes, including those associated with muscles, most articles still refer to the articular cartilage lining of freely moving joints such as that at the knee as the key tissue that fails over time and is impervious to intervention because once diseased the tissue inevitably degenerates [4]. At the same time, several studies that focus on the molecular changes in osteoarthritis and/or possible disease modifying drugs to counter cartilage pathology do not appear to embrace any clear role

for any form of muscular antecedent or mediating factor in the disease cycle [5].

Since the body of research directed towards the search for a viable form of osteoarthritis mitigation is currently limited in this regard, we propose it may be useful to examine the idea that osteoarthritis may stem in some cases from the prolonged interaction of subnormal reflexive interactions between muscles that may be infiltrated by fat or other non-contractile components and their reduced strength and adverse joint based tissue mechanical and physical stresses and strains [6]. This idea is not novel, but is one that accepts, rather than ignores, the innate ability of the human motor and skeletal systems to respond adaptively to diverse biological stimuli including deficient, subnormal or excessive joint and/or associated muscle or soft tissue impacts [7,8]. It was hence felt an updated review and one that acknowledges the close links between form and function, injury and mechanical loading effects might lend some needed insight into the disease origins and its variations. Muscle was the focus of this discourse because i) it is possible the focal distribution of osteoarthritis may be mediated by muscle mechanisms, ii) muscle starts to undergo structural age associated attritional changes quite uniformly, iii) treating muscle appears to be one aspect of osteoarthritis that appears respond to its practice and is a low cost factor that can generally be safely examined, measured, intervened upon and improved.

Aims

To extend what is known in this regard, this current report aimed to specifically examine if the idea that some forms of osteoarthritis may represent an adverse adaptive response of one or more joint tissues to one or more insults, in the face of deficient or unrelenting subnormal reactive and protective muscle mechanisms this report aimed to summarize what trends exist in this regard. Indirectly, it strove to provide support for the idea that carefully tailored interventions designed to improve one or more aspects of muscle function may set the stage for joint healing or disease retardation and with this more favorable rather than adverse outcomes.

Tested in this respect is the idea that osteoarthritis and its numerous molecular and biochemically deranged compositional, biomechanical and metabolic features may emerge as a structural-functional adaptation or autonomous temporal response to a variety of cascading extrinsic as well as intrinsic injurious stimuli that may manifest more readily in an older person than a younger person. If this premise is valid, as outlined schematically in Fig. 1, it may account for- as well as induce- those progressive and disabling cortical, sub-cortical, spinal segmental, muscle and joint level forms of atypical functional and structure observed in osteoarthritis.

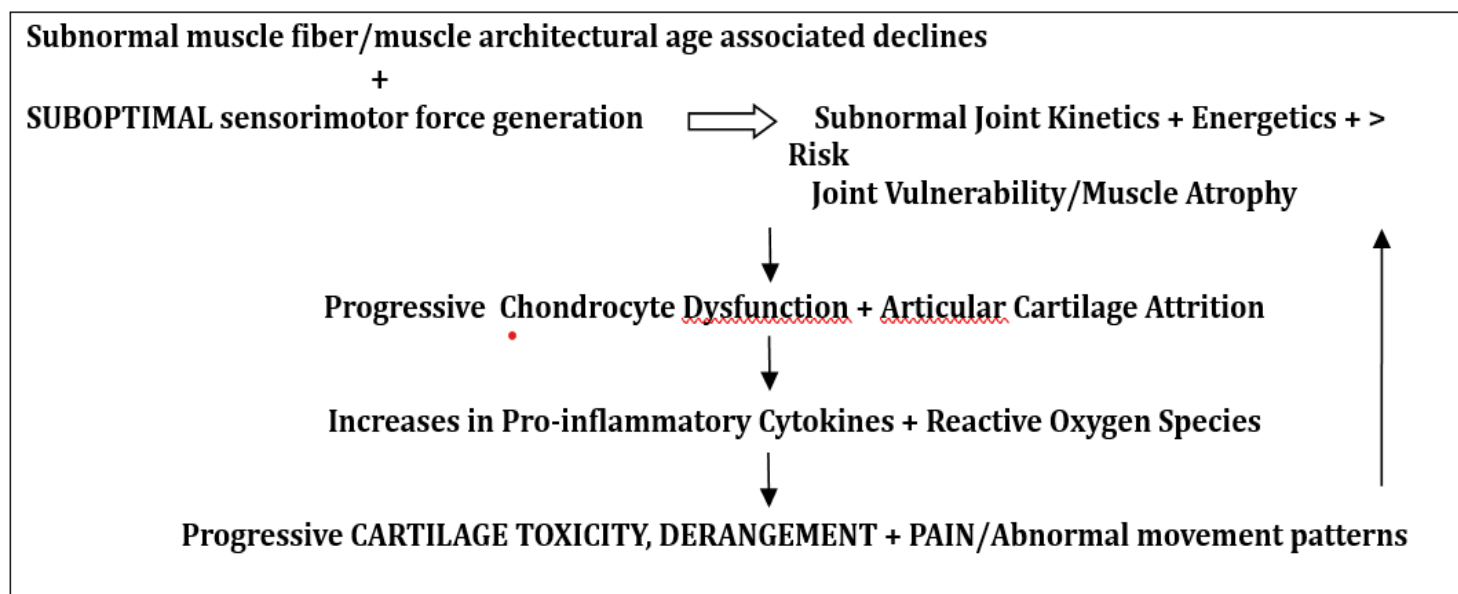


Figure 1: Hypothesis tested through this current narrative review.

Methods

To achieve these abovementioned review aims, we elected to build on an extensive review of available documents housed in PUBMED, PubMed Central and Google Scholar from 1990 up until 2019 using the key terms: Osteoarthritis/Muscle/Muscle Atrophy/Muscle Dysfunction/Muscle Impairment and Muscle Pathology. More specifically, an updated overview of related research published between January 1, 2020-July 31, 2024 was sought.

To this end, all available articles on these websites were scanned for relevance and selected for further review if the article addressed some aspect of the current topic of interest without regard to research design. An attempt was made to include all modes of inquiry, but the focus was on their clinical or theoretic contributions. No systematic review or crucial analysis was conducted as the topic at hand was found too diverse and non-uniform. Moreover, while it is acknowledged the body of data may not be exhaustive-it does arguably reflect most of the current muscle associated osteoarthritis research studies and their tentative conclusions using three reputable data bases, taken to presumably house and capture the state of the art and gold standard peer reviewed papers on this topic sufficient for arriving at a reasoned opinion through a narrative lens. Readers can learn more by exploring the current cited reports as well as some prior reports, for example Chen, et al., De Ceuninck, et al., Suter, et al., and Shiavi, et al., [9-12]. This paper does not discuss any specific form of osteoarthritis or surgery associated studies. No exercise or intervention studies were examined unless muscle pathology was discussed.

Results

General Observations

Among the literature currently posted and reviewed, it is evident many studies published in recent years discuss the epidemiology and costs of osteoarthritis to society, but very few offer any definitive explanations as to why osteoarthritis is increasing in prevalence and why so few efficacious approaches for mitigating this widespread disease in any population have been demonstrated to date. No longer considered a disease of articular cartilage alone, osteoarthritis, which induces or is induced by abnormal bone remodeling processes and some degree of joint swelling and joint inflammation its link to muscle as a causative agent or even as an emergent mediating agent is commonly less well accepted and articulated [13]. This is surprising because several early studies link osteoarthritis to induced injury wherein related muscle mechanisms are clearly associated [12-14]. In addition, more recent insights regarding an age associated pathological state of muscle weakness and muscle mass loss termed sarcopenia, that is quite common and has a bearing on muscle strength and function has been cited as a possible prevalent factor in the older adult osteoarthritis population that may be fostering and account for its onset as well as its progression.

In line with past literature, current evidence also strongly implies that declines in muscle strength associated with osteoarthritis, also accompany the pain experience, alterations in joint stability, maladapted postures, excess force production and defective neural reflex responses and neuromuscular transmission and reception processes [14]. In addition, it appears cellular and molecular level changes in cartilage chondrocytes as well as muscle myoblasts share a common set of pathological targets and muscle quality pathways that could explain their impact on osteoarthritis risk and outcomes, even in the face of joint replacement surgery [10,15].

In particular, the presence of forms of dysfunction within the neuromuscular system may set the stage for cartilage, bone, synovial membrane and capsular changes, plus the production of inflammatory cytokines subnormal limb kinetics and kinematics and various muscle structural alterations that are hard to reverse [16-18]. For example, alterations in one or more of the highly complex network of sensory nerves that normally serve to coordinate joint mobility and stability can undermine joint biomechanics, movement efficiency, limb posture, joint stability and functional ability as can muscle inflammation, muscle fiber degeneration, muscle blood flow alterations and joint effusion [19-22].

Mansfield, et al., found individuals with osteoarthritis of the knee to not only have motor deficits associated with decreased neural activation and central nervous system sensitization, but decreases in quadriceps muscle spindle responsiveness, along with increased calf muscle activity [23]. Ling, et al., implicate muscle activation changes at the motor unit level in the context of symptomatic knee osteoarthritis that is mediated by radiological disease severity [24]. Recently Schaefer, et al., reported strength deficits of hamstrings patients with knee osteoarthritis wherein the more affected side seemed to show further specific impairments regarding neuromuscular control [25]. This research is fairly novel and as indicated recently by Lopes, et al., should

not be ignored as there may be more to the pathology of knee osteoarthritis and its muscular associations than is widely acknowledged, such as possible deficits in muscle rate of force development [26,27].

Additional Observations

In addition to the aforementioned muscle associations studied in the context of the osteoarthritis disease cycle - it appears muscle weakness or wasting or both found in osteoarthritis may also serve as possible disease causative or progression factors that encroach on independence, joint mobility and stability [11,28]. Moreover, a role for reflex muscle inhibition and poor muscle activation patterns consequent to joint inflammation as well as joint destruction can be considered as probable and serious osteoarthritis pathogenic correlates, regardless of whether these are reactive or causal [24]. Pain and related immobility responses that promote muscle disuse atrophy and weakness, poor muscle quality, muscle fat infiltration and increased muscle stiffness are additional muscle related pathogenic mediators or moderators as are alterations in muscle architecture and morphology plus muscle volume losses and muscle inflammation [29-33].

Other reports imply muscle fatigue/poor muscle endurance may be expected to foster rather than retard damaging bouts of joint loading and load distribution and strain [34]. Similarly, a general or selective loss of muscle-based enzyme production and functional losses may have an independent or cumulative bearing on joint loading deficiencies and aberrations [35]. In particular, decreases in timely as well as appropriately modulated voluntary activation efficiencies, may hasten its progression quite markedly and significantly as may muscle weakness, inefficient bouts of appropriately modulated muscle force production, alterations in muscle growth differentiation factor, abnormal movement synergies, muscle atrophy and disuse, muscle size declines and a proportionate change in non-contractile muscle tissue presence, even if one or more of these observed changes or deficits are unevenly manifest and observed across different muscles and degrees of pathology [35-44]. Other recent examples of muscle joint interactions that may play a pivotal role in cartilage damage and irreversible alterations of articular cartilage biochemistry plus variable responses to joint damage and surgery are: muscle based circuits associated with protein degradation and fibro-adipogenic cell gene expression, muscle inflammation and altered gene muscle dysfunction [45]. In addition, differential muscle activation patterns and excess or suboptimal joint stiffness may mediate osteoarthritis progression and severity [32,46-50]. Other factors that can play a unique or additive role in osteoarthritis progression are various degrees or combinations of muscle fiber and whole muscle atrophic and degenerative changes or transitions. The presence of sarcopenia involving a loss of muscle mass and strength, muscle atrophy, possible impairments in neuromuscular innervation and muscle composition can likewise be expected to further impair muscle quality and function as well as functional ability, muscle and joint tissue regenerative capacity and comfort levels and should be examined further in the future to better establish any causative or clinically relevant linkages [40,51-56].

In short, even if somewhat inconclusive, as outlined above, it appears joint status at any age may be degraded progressively in some respects as a result of preexisting and/or emergent muscle deficiencies or abnormalities that impact the efficiency of static or dynamic joint loading efforts. These include, but are not limited to a) Those residing in or influencing the central, spinal and peripheral nervous systems; b) Those due to alterations in muscle contractile properties, muscle quality, muscle fat content, muscle transcription factors and selective muscle fiber losses, rearrangement, derangement, transitions or maldistribution; c) Those due to persistent abnormalities in muscle reflex activity and force production, muscle agonist/antagonist imbalances and contractures, uncoordinated and muscle force timing and directional changes; d) Those due to muscle inhibition, inflammation, impaired muscle metabolism and microcirculation; e) Those due to muscle pain, muscle injury and subnormal muscle afferent and efferent transmission and reception deficits; f) Those due to muscle disuse, abnormal motor unit activation, muscle fatigue, muscle co contraction and uncoordinated movement patterns and their impact on joint, bone and surrounding supportive tissues; g) Those due to unresolved or poorly treated cardiovascular conditions and obesity; h) Those due to poor nutrition and vitamin D intake or exposure.

On the other hand and accepting the obvious shortcomings of this report that did not cover the bulk of literature published before 2019, the majority reported here were taken to represent the key peer reviewed studies and comments published in English in 2024 over the last five years and that have detailed various muscular abnormalities in the context of osteoarthritis onset or its manifestations among older adult populations. As hypothesized in Fig. 1 and regardless of research approach or issue examined and that many other factors may be involved, when viewed collectively, it appears most current authors as well as those that

have led this line of research study indicate this hypothesis may have some bearing on osteoarthritis and is worthwhile to pursue in the future. Even if the idea is eventually refuted, if such research is well designed it can yet help reveal how osteoarthritis emerges in some cases and not others, rather than jumping to well-trodden and repeated conclusions that may not pertain universally. This line of inquiry is encouraged however because it is likely have the potential to reduce suffering and the immense costly osteoarthritis burden over time. Even in 2024, some clinically beneficial applications and insights and conclusions appear highly promising [78].

Discussion

Despite over a century of study, osteoarthritis the most common form of arthritis and an immense disabler of older adults, is hard to mitigate effectively. Frequently described a disease of articular cartilage, it is accepted as being a progressive disease with few options for effective remediation or mitigation. We thus asked ourselves whether this is because osteoarthritis is indeed inevitable or are there other factors that have a salient disease influence such as failure of inherent joint protective mechanisms. The rationale for this aforementioned line of thought, while not conclusive, has been and is currently supported to a modest degree in our view by varied evidence that has emerged of multiple reflexive oriented and other underlying or emergent adaptations of the motor system that appear linked to the disease progression or its persistence and severity. However, since the force generated by muscle is attributable to muscle cross sectional areas and level of motor unit activation, if muscle abnormalities remain unaddressed or overlooked in the clinical realm as well as the research realm, it may be challenging to fully comprehend the nature of osteoarthritis pathology and its required treatment and especially optimal treatment.

In particular, if there are one or more influential osteoarthritis-muscle linkages that remain undiscovered or untreated, both prevailing possible adverse compensatory muscle mechanisms as well as neural reflex responses may well exacerbate joint attrition processes quite significantly. At the same time, the presence of undetected and untreated muscle weakness, including sarcopenia and/or excessive muscle fat infiltration processes may be increased along with joint vulnerability [6,41,57]. Indeed, as some studies show-associated preexisting or progressive sensorimotor input impairments and their impact on muscle force production abnormalities and strength declines may help to explain the cycle of joint instability and abnormal kinematic patterns and joint kinetic responses often reported among severely disabled as well as minimally disabled osteoarthritis cases (Table 1) [38,58-60].

Researchers	Noteworthy Findings
Brightwell, et al., [43]	In patients, muscle growth differentiation factor predicted atrophy, weakness and peri articular bone loss six months following surgical ligament reconstruction-a known osteoarthritis precursor In mice, the researchers found that the antibody of this factor substantially mitigated muscle atrophy, weakness and fibrosis and rescued the skeletal muscle and articular cartilage transcriptomic responses to the ligament injury The strategy also attenuated the degree of post traumatic osteoarthritis severity and emergent deficits in the periarticular bone microarchitecture
Cigercioglu, et al., [7]	Knee and ankle muscle architecture, knee extensor muscle force and plantar pressure distribution in the dominant foot differentiated study individuals with knee osteoarthritis from the matched controls
Drummer, et al., [44]	Muscle inflammation appears to have a potential regulatory impact on endothelial cells within skeletal muscle that could impact muscle and joint performance
Ericsson, et al., [45]	Having stronger thigh muscles four years after meniscectomy was associated with less severe osteoarthritic medial tibiofemoral compartment changes of both the operated and contralateral knee 11 years later
Gong, et al., [13]	Muscle composition/neural factors may explain the reductions in muscle strength and variation in symptoms in people with midfoot osteoarthritis
Hatfield, et al., [47]	Muscle activation patterns and strength explained significant variance in moment difference and were highest for the knee flexion moment and could alter dynamic loading patterns associated with knee osteoarthritis

Lee, et al., [48]	Severe psoas muscle atrophy as observed in hip osteoarthritis is related to lower extremity pain, even if there is a coexisting lumbar spine pathology
Kameda, et al., [69]	Gluteus medius syndrome appears related to lumbar spine degenerative disease, hip and knee osteoarthritis and failed back surgery syndrome
Lee, et al., [51]	Leg muscle asymmetry in men is associated with a significantly higher grade of radiographic knee osteoarthritis than controls
Li, et al., [79]	Aberrant fibroblast growth factor signal transduction is associated with various pathological conditions such as cartilage damage and may promote osteoarthritis cartilage degradation processes
Li, et al., [32]	Higher degrees of dynamic joint stiffness, lower quadriceps strength and greater quadriceps stiffness are risk factors for knee osteoarthritis in the older adult
Peng, et al., [83]	Sarcopenia is associated with the onset of osteoarthritis in older adults
Shang, et al., [80]	Treadmill exercise alleviated the atrophy and degeneration of muscle fibers in post traumatic rat osteoarthritis, the degradation of muscle fibrin and articular cartilage and subchondral bone loss.
Tuna, et al., [59]	Isometric knee flexor + extensor strength correlate with femoral cartilage thickness

Table 1: Selected observations regarding a role for muscle in osteoarthritis disease trajectories.

In sum, while Table 1 is not designed to convey the many parallel studies that echo its conclusions, it is taken to depict the trends in the current literature and possible importance of continued efforts to examine the potential significance of one or more motor alterations as explanatory factors in the osteoarthritis disease cycle as this occurs among the older adult population. Indeed, this current review consistently shows most authors had substantive findings of clinical relevance even with limited samples and almost all presently advocate for more advanced and supportive studies and studies that do not preclude a thoughtful combination of muscle related variables assessed routinely and with more contemporary tools. Emergent research also supports the view that establishing the relative importance of epigenetic as well as intrinsic muscle genetic alterations as this impacts muscle fiber pathology or loss, muscle fat mass, muscle inflammation, effusion and deficient muscle circulation, plus muscle growth differentiation and functional performance and weakness factors as possible osteoarthritis determinants will prove insightful [28,43,44].

In the broader sense and realm of public health practice and resource allocation and goals to foster healthy aging, despite more prevalent osteoarthritis predictions, it appears efforts to more succinctly describe potentially mutable osteoarthritis disease determinants and transitions, including muscle are highly desirable. In this sense, ample evidence shows that the cycle of events shown in Fig. 1 may be sufficiently salient to further explore, especially if muscle fiber size impairments, as well as muscle quality and quantity can be improved and with this joint function as well as life quality and possibly a higher chance of more favorable surgical outcomes in severe cases, attenuation of early osteoarthritis and mild symptoms, more favorable cartilage regeneration processes, less pain and fewer muscle strength asymmetries and extent [42,46,61-72].

In the interim, it seems safe to say those suffering from sarcopenia and muscle atrophy who may be subjected to multiple bouts of persistent joint loads that prevail during activities should be targeted, especially if multiple muscles are implicated [74-77]. As a result, a high number of older osteoarthritis cases may be able to avoid unsafe remedies or a need for narcotics commonly used to relieve their pain and that may actually generate dysfunctional muscle synergies, retard sensorimotor reflex responses and foster abnormal joint kinetics [73]. Alternately, regardless of whether muscle dysfunction predates or emerges in the context of osteoarthritis, their early timely detection, their accurate differentiation and classification and disease relevance, plus possible long term targeted treatments or normalization procedures to avert physical inactivity and its impact on joint stiffness and reduced tendon, ligament, muscle extensibility and flexibility [84], may prove highly beneficial in averting or minimizing joint pathology [76,78-85]. It is our further view that precursors of muscle dysfunction in the population in general such as obesity, injury, sedentary lifestyles and poor diabetic control may also warrant attention and could be studied alongside diverse osteoarthritis cases and healthy adults in the community and should be addressed accordingly if deemed of apparent salience.

Conclusion

Despite disagreements over the actual initiating factors underpinning osteoarthritis, it is evident that a role for neuromuscular factors in the osteoarthritis disease cycle cannot be readily dismissed. It is further concluded that if more research is undertaken, examining muscle attributes alongside anthropometric, functional, biochemical, molecular, cellular, inflammatory and radiologic attributes concurrently will greatly enhance associated disease understandings and intervention and treatment implications.

On the other hand, we conclude a failure to fully understand how factors such as muscle imbalances, muscle contractile delays, as well as muscle weakness and poor endurance, among other muscular related problems common in aging and osteoarthritis may limit a complete disease understanding and is likely to influence the disease process and its disabling features adversely and place more rather than less demands on health care systems and personnel and families.

Indeed, current and future practitioners who take the time to reflect on the following evidence-based observations and emergent data regarding what we know of muscle contributes to structural and functional joint changes may be able to help clients to confidently control or minimize their pain and avert unwanted social and fiscal costs. Researchers can help immensely in this regard by validating and expanding upon the degree to which the findings summarized below can be supported and extended:

- The role of possible defective muscle transcription influences
- Muscle fiber transitions, derangement and atrophy
- Muscle protein degradation and architectural alterations
- Muscle stiffness and suboptimal muscle shock absorption capacity
- Muscle ischemia, inflammation, tenderness and effusion
- Muscle quality and disproportionate fat mass presence
- Muscle spasm, imbalances and contractures
- Subnormal muscle spindle responses, endurance capacity and muscle weakness
- Sarcopenia and muscle injury
- Muscle asymmetry from side to side and among agonists/antagonists

Final Comments

It is our belief that until more knowledge and effective osteoarthritis treatments are forthcoming, exploring and examining patients to identify any of the above muscle attributes will be highly beneficial and may avert widespread movement alterations and discomfort, as well as fatigue and an unwillingness to exercise consistently. In addition, if patients understand why they may have to exercise in a particular way and what this may entail, they may well favor such treatments. At the same time, generic exercise recommendations that may do more harm than good if these are non-specific and not carefully tailored or titrated according to their age and degree of pathology and level of overall health should be avoided. By routinely carrying out simple clinical tests practitioners can help to uncover their patient's specific needs and deficiencies. As such, they can arguably make a sound contribution to reducing the osteoarthritis burden, while expanding the effectiveness of their practices - as well as attempts to restore cartilage and foster independent high-quality lives and the ability to function physically, socially and even economically.

Conflict of Interests

The author declares that he has no conflict of interest in this paper.

Ethics Approval / Institutional Review Board Statement

Not applicable

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