

# Muscle and Muscle Mechanisms as Possible Factors Leading to Osteoarthritis

Ray Marks\*

*Department of Health and Behavior Studies, Columbia University, USA***Article Information**

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**\*Corresponding author**

Ray Marks, Department of Health and Behavior Studies, Columbia University, New York, USA, Tel: 1-212-678-3445; Fax: 1-212-678-8259; Email: rm226@columbia.edu

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**Abstract**

Osteoarthritis is a disabling disease with no known cause. The role of muscle dysfunction as an etiological factor has however been discussed, and evidence in favor of this hypothesis has recently been sought. This brief highlights some research in this respect and offers some directives for clinicians and researchers interested in reducing the osteoarthritic disease burden based on these observations. Among these data drawn from the major databases housing reports aligned with this topic, a reasonable body of basic scientific evidence indicates that suboptimal muscular contractile forces, as well as the presence of disordered muscle physiology may adversely impact articular cartilage structure and function. Second, a variety of clinical studies show surprising muscle related abnormalities in the context of osteoarthritis that are not explained by age, or pain alone. Others suggest treatments directed towards improving muscle function in those with symptomatic osteoarthritis can produce favorable results. Others show, that despite treatment to improve joint status in those with osteoarthritis, muscle function may not improve, even when pain is diminished. These varied findings indicate more research in this area could prove fruitful, and that attention to examining and treating muscle directly or vicariously is likely to prove more useful than not among people with osteoarthritis.

This brief originates from a very extensive search of the available database concerning the possible predisposing factors underlying osteoarthritic joint changes, plus factors which may be involved in producing progressive osteoarthritic joint damage, once the disease process is present. As practitioners, this knowledge is critical to improving our present limited ability to effectively treat osteoarthritis, the most prevalent joint disorder, and thus the leading cause of joint pain and joint disability throughout the world.

As well, this knowledge is absolutely essential to improving our present limited ability to effectively initiate preventative strategies against the disease and its progression which might considerably reduce the magnitude as well as the economic and social costs of this disabling disease. Unfortunately, despite a large amount of related research, and the possibility that pathology of the neuro-motor system may promote joint dysfunction and hence may be an important target treatment area for clinicians, the precise causes and factors influencing osteoarthritis, still remain in question.

Indeed, while every clinician recognizes symptomatic osteoarthritis when they see it, the precise explanation for the underlying causes of these symptoms, plus the ability to accurately predict the natural course of the disease is unclear. The direction needed to ameliorate and/or prevent osteoarthritis remains essentially obscure [1].

Nonetheless, during recent scientific meetings concerning the causes of osteoarthritis and its progression, some interesting ideas have emerged which suggest some forms of the disease may be caused by an imbalance between the physical stresses placed on the joint tissues and the inability of these tissues to withstand these stresses, as well as all the structures of a joint [2], including muscle [3]. In addition, implicated in cartilage breakdown due to abnormal physical stresses are those attributable to anatomic and developmental deformities, obesity, trauma, bone micro-fractures and bone remodeling, plus joint instability, which could all, in turn, be caused by failure to generate the required muscular forces at a given point in time during an activity, by uncoordinated muscular forces, by lack of adequate muscular force [3,4], by site specific excessive muscular forces [5-7] or by muscle contractile dysfunction [8]. Processes such as neurogenic muscular atrophy, muscle fiber degeneration, and regeneration might also contribute as cofactors to the development or progression of the disease as suggested by Fink et al. [9].

Another important finding is that since the synthetic and degradative processes of normal articular cartilage are maintained, in part, by intermittent loading imparted to the articular cartilage

chondrocyte, it is likely that abnormal alterations in this respect, such as static loading or no loading [10], or various degrees of joint impact injuries [11] may produce disturbances of cartilage metabolism that lead to chondrocyte death, cartilage loss and eventual loss of joint function even in a joint with normal articular surfaces, alignment, stability, innervation, and muscle control.

In view of these possibilities, it thus seems plausible to suggest that in addition to static factors, abnormal dynamic forces imparted by muscle may play an extremely important, if not pivotal role in producing cartilage damage that lead to cartilage loss. That is, alone, or in combination, both too much muscular force or too little muscular force may affect articular loading detrimentally such that the increased or diminished load on the articular surface could cause an irreversible alteration of articular cartilage biochemistry [12].

In contrast, mitigating against age, which has previously been considered the major cause of osteoarthritis is the observation that not all older people have the disease, even if they have radiographic evidence of joint space narrowing. In addition, many symptoms and signs of osteoarthritis can be found on careful questioning and clinical examination in young adults and even in children, for example, those with knee malalignment. In other cases, older patients may indeed experience a remission of their disease.

Also, at the knee for example, many cases of osteoarthritis occur unilaterally, not bilaterally, as one would expect if age alone was the causative factor. As well, age cannot explain how degeneration is often confined solely to one area of a joint surface and why osteoarthritic cartilage is not the same as aging cartilage. Finally, since joint surgery which reduces pain and provides a sound mechanical surface does not always improve an osteoarthritic patients function, nor their strength capacity or rate of muscle force production [13], and is often followed by a re-occurrence of symptoms or surgical failure, it is highly likely that other factors must be considered as contributory to the osteoarthritic disease process and possibly to its initiation and progression. The same arguments can also be applied against most genetic and systemic explanations of osteoarthritis.

## Objective

Because the possibility that disturbances residing in the neuro-motor system may increase the risk of incurring osteoarthritic joint disease [14], and the important implications of this possibility for clinicians, this brief focuses on evidence which supports this viewpoint. While it is prudent to also weigh contradictory evidence against this hypothesis, it can be stated that very little evidence could presently be found to the contrary, when reviewing the current literature on this topic published in peer review journals over the last 10 years. Using the Web of Science, PUBMED, and Scopus databases and the terms muscle and osteoarthritis, muscle fatigue and osteoarthritis, muscle spindles and osteoarthritis, muscle dysfunction and osteoarthritis at least 75 supportive articles related to this topic with many focusing on some aspect of muscle structure or function as a possible contributing factor to the development and progression of osteoarthritis were accessed and reviewed. This does not include foreign language publications or those published in preceding years.

## Findings from the Related Literature

### General observations

Among the literature retrieved from the aforementioned databases, a thematic analysis revealed a highly diverse body of evidence on this topic despite almost 25 years of related research. However, among the very broad array of studies that were reviewed and met criteria, several lines of evidence supported the idea that osteoarticular damage can be caused or magnified by a variety of muscular mechanisms, including the generation of abnormally excessive muscular forces, as well as those which result in an inadequate muscle force generation. In terms of the characteristic focal areas of cartilage damage occurring in osteoarthritic joints, the diverse body of research presently available also provided tentative support for the view that these might be produced by focal alterations of force placed on cartilage by muscular related force generation imbalances, rather than overall joint loading effects. These include, but are not limited to the excess force production due to muscle spasm [15], muscular contractures [16], muscle weakness leading to abnormal movement patterns [17,18], muscle inflammation [19], and impaired muscle afferent activity [e.g., 20-24].

Yet others suggest poor muscular coordination, especially a reduced ability to generate eccentric muscle forces in a timely manner, a normal mechanism for attenuating high impact joint forces, may produce subchondral bone fractures, which leads later on to further reduction in joint shock absorption capacity and cartilage damage [25]. Moreover, more immediate cartilage damage may ensue if the initial impact load is sufficiently high, and the muscles fail to protect the joint, as outlined by Agostini et al. [26]. In addition, skeletal malalignments that often seem to associate with osteoarthritis may be due to early muscle imbalances and progressively abnormal dynamic muscular force adaptations which alter joint reaction forces abnormally as suggested by work by Matsumota et al. [27] and Pan et al. [28]. As well, even if not necessarily involved in the onset of osteoarthritis, afferent sensory dysfunction, along with diminished strength capacity may have a role in mediating the disease progression [29]. The finding that muscular paralysis of the other hand may be protective against osteoarthritis development on the affected side in the hemiplegic patient, but may hasten joint degeneration on the contralateral side [30] strongly implies the role of muscle in the osteoarthritic disease process is complex and should not be underestimated.

Metcalfe et al. [31] found the patients with unilateral knee osteoarthritis do experience abnormal loads of their major weight bearing joints bilaterally, and these abnormalities persist despite treatment of the affected limb. The findings of this group suggested that the presence of either pre-existing muscle pathology and /or an alteration in afferent input to the central nervous system and long term adaptations may prove detrimental to articular cartilage in vulnerable joints such as the knee. This idea was recently supported by Oiestad et al. [32], who conducted a systematic review and meta-analysis that showed knee extensor muscle weakness increases the risk of developing knee osteoarthritis in both men and women.

## Additional study findings

Recently, Amaro et al. [33] who examined gluteus medius atrophy relative to contralateral and ipsilateral hip osteoarthritis, concluded gluteus medius muscle weakness on one side of the body may predispose the unaffected contralateral hip to developing osteoarthritis. This conclusion was also supported in a basic study by Renhan et al. [34] who reported that muscle weakness caused joint degeneration in the rabbit, and by Wang et al. [35] who found muscle cross-sectional area and cartilage volume were positively related. Amin et al. [36] in contrast, found greater quadriceps strength protected against cartilage loss at the lateral compartment of the patellofemoral joint, not at the tibiofemoral joint.

Ling et al. [37] who found changes in motor unit physiology associated with early knee osteoarthritis correlated with the degree of radiographic severity, also reported muscle strengthening may not always protect an individual from osteoarthritis. They suggested there is a more complex association of muscle function and joint physiology than simply a reactive one.

In this regard, DePalma and Gilchrest [38] who observed the unanticipated presence of unilateral thigh atrophy and weakness in a case of hip osteoarthritis, suggested muscle should be viewed as a possible mediator of osteoarthritis. Given its role as both an afferent and efferent structure that not only produces movement, but relays proprioceptive information that promotes function, joint stability, and shock absorption, this argument does seem like one is meriting further exploration. In support of this viewpoint, early work by Messier et al. [39] implied that the presence of any uneven declines in quadriceps and hamstring strength surrounding a knee joint could sensitize an individual to the detrimental effects of high impulse loads more highly than if the muscles were well balanced and coordinated temporally and in magnitude since the muscles are important shock absorbers. This exposure of the cartilage to excess loading impacts can produce cartilage damage, which, in turn, produces reactive effects on the knee joint, muscle structure and function that perpetuates the condition. Unsurprising therefore, Omori et al. [40] who examined the relationship between radiographic knee osteoarthritis and quadriceps strength found a systematic correlation between the presence of this joint condition and the magnitude of the prevailing decline in quadriceps strength. Furthermore, it was suggested that the decline in quadriceps muscle strength may be more strongly related to the incidence of knee osteoarthritis than to its progression.

In cases of patellofemoral joint osteoarthritis, Stefanik et al. [17] too found quadriceps weakness correlated with the extent of cartilage damage and underlying bone marrow lesions, and in women with hip osteoarthritis, Tsarkoma et al. [41] found these women who exhibited strength asymmetry of crucial hip muscles as well as near zero correlation between important agonist muscles, also displayed the degree of balance and coordination needed for dynamic actions like gait to be optimally functional. The presence of any inter-limb asymmetry during walking and other weight bearing functions, coupled with persistent differential intra-limb muscle force generating capacity can predictably foster abnormal wear and tear and disrupt both cartilage physiology and its structure at one or both hip joints and others.

As evidenced in animal models studied closely by Herzog and Longino [42] muscle weakness alone can independently

increase

## Implications for research and practice

Although there is no clearly consistent body of literature that can answer the question about the temporal link between muscle and joint structural changes in osteoarthritis due to the varied samples studied, the varied muscles studied, the varied joints studied, and diverse methodological approaches, as outlined in Table 1, a wide variety of recent studies and study approaches do provide some tentative support for continuing to examine the importance of muscle in the osteoarthritic process in the future. In particular, based on recent data, muscle fatigue and muscle strength are clearly very important modifiable correlates of osteoarthritis that can be improved clinically in most cases. Others studies showing the negative effects of ipsilateral and contralateral muscle asymmetry, both structural and functional [e.g., 79,83], and the potential importance of the ability of muscle to contract in both a coordinated and timely fashion [e.g., 79] also speak to the importance of assessing these aspects of function in the patient with both early and late stage stage osteoarthritis. Measuring muscle volumes [83], which appear associated with the extent of pathology [71], plus morphologic muscle changes said to be indicative of neuromuscular adaptations [23] might help to pinpoint where the intervention emphasis might lie. Indirect evidence that treating muscle, does improve function in some instances, further suggests the mechanisms for this should be explored, and early rather than late intervention is warranted because muscle does not respond to late stage intervention in all cases.

In short, it is the authors' view that early careful neuromuscular and biomechanical assessments and subsequent interventions directed to the optimization of muscle strength, cross-sectional area, fiber type distribution and diameter, endurance, as well as synergistic aspects of muscle function, optimal co-ordination, muscle agonist antagonist balance, and responsiveness and rate of force development as indicated, may not only greatly alleviate the disease burden, but it may prevent or allay the condition and/or the extent of any ensuing additional joint involvement and deterioration. In addition, if this hypothesis is supported in the future, it would, at least, provide a possible avenue for more optimal surgical outcomes as well as non surgical outcomes for people with osteoarthritis than is presently observed. Indeed, as outlined by de Ceunink et al. [51] the consistent body of evidence showing that a decline in lower limb muscle strength is associated with knee or hip osteoarthritis may lead one to conclude that chondrocytes and myoblasts share common pathological targets and pathways, and that the potential advantage of understanding this association has far reaching clinical implications. In addition, the finding of differences in the organization of the motor cortex in adults with and without osteoarthritis [74] suggests that the motor pathways may be implicated in motor disturbances associated with some forms of osteoarthritis, and thus unless this is acknowledged, it may be difficult to improve muscle function after corrective joint surgery in all cases [13]. The array of factors that could be examined and appear to interact negatively on joint status are shown in Figure 1.

## Conclusion

Osteoarthritis is a burgeoning health care problem with immense adverse impacts of the individual and societal levels. Bearing in mind the considerable research and linkages between muscle and important

correlates of the disease outlined in Figure 1, even if osteoarthritis cannot be prevented, it appears efforts to assess and improve muscle function where indicated can at a minimum potentially retard the extent of degeneration that might otherwise occur at the osteoarthritic joint and others [52]. Muscles and their myokines are also increasingly being found to exert local effects on muscle in response to activity, as well as general endocrine effects implicated in chronic diseases [80]. To this end, research that incorporates biological and biomechanical examination of the muscular system, as well cross sectional and longitudinal efforts to examine the state of the musculature more closely than is currently the case in the clinical setting, including that of the unaffected side in unilateral cases, and intervening to offset any remediable muscle abnormality is strongly recommended. Intervention approaches applied individually, or collectively, as indicated, might follow thereafter, and might include:

- Electrical muscle stimulation.
- Endurance exercises.
- Muscle vibration [53].
- Electromyographic biofeedback controlled exercise.
- Active range of motion exercises.
- Daily passive muscle stretches.
- The use of assistive or orthotic devices.
- Strength training designed to optimize muscle timing and size [6,35,52].
- Yoga therapy [54].
- Weight loss or weight control.
- Modalities that minimize pain and muscle spasm.
- Efforts to minimize joint effusion and muscle inflammation.
- Promoting vitamin D intake or exposure as this effect the muscle function.
- Sensori-motor training.

Finally, in terms of evaluation, the present data also imply that this should not be limited to an orthopaedic examination of the symptomatic joint site, but should include careful neuromuscular examination of the affected joint(s) plus those of the lumbar and the cervical spines where sensory input that controls movement is located. Patients prone to depression that may foster sedentary behavior or excess weight gain or excess pain should be counseled about the importance of daily physical activity to promote joint health. Conversely, if a patient is not responding to conservative treatment after several weeks of intensive continuous treatment or is showing declining function the clinician may advocate sensory and/or motor nerve conduction tests to eliminate the possibility that this is not due to irreversible damage in the neuro-motor system. Finally, early intervention is strongly indicated to offset the chances for developing learning movement patterns that are compensatory or abnormal and that seem resistant to recovery [55] even after the pain is relieved as these may foster further adverse joint adaptations.

It may also be thought that until we are better informed respecting the nature of osteoarthritis that the opportunity for effective remediation for this disease will remain poor as was recently demonstrated in pre-surgical physical therapy outcomes, which were not maintained after surgery [56], or which left exercising patients worse off post-surgery than those receiving no therapy at all [57].

Having a better understanding of all the mechanisms that might contribute to the disease, especially those that underlie the motor abnormalities found in osteoarthritis may provide hope for minimizing the immense burden of this prevalent disorder, as well as for improving outcomes. In particular, the ability to both intervene as early as possible and to apply well-reasoned evidence-based specific approaches rather than broad generic solutions, is likely to prove highly efficacious in ameliorating this disabling health condition. Since different muscles may undergo different types of pre- or post-arthritis change, different treatment approaches may be desirable at different time periods for minimizing problems at a single joint site and at distant joint sites. As well as more sophisticated clinical examinations that can guide the clinician more ably, the ability of clinicians to better understand how to intervene to foster optimal muscle is desirable. Imparting these understandings to their osteoarthritis patients may also help to secure more successful outcomes in the long run [58], as well as their heightened cooperation to pursue the long and continuous rehabilitation commonly required, particularly in those with mild to moderate osteoarthritis. While encouraging those at risk for the disease to be equally compliant is also highly recommended, care must be taken against doing more harm than good due to excessive exercise or joint use. Some approaches for assessing the status of muscle and its correlates and some correlates of neuro-motor function that may be implicated in the osteoarthritic process are shown in Boxes 1 and 2. Those evaluations outlined in Table 1 should be conducted on involved and uninvolved sides and involve proximal and distal muscles where indicated [84,85].

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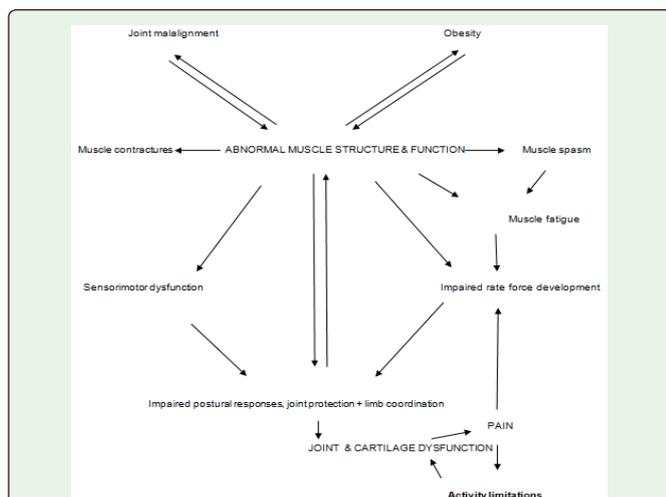


Figure 1: Hypothetical interaction of muscle and joint health and joint degeneration.

**Table 1:** Selected studies reported in the last 10 year, suggesting a wide variety of neuromuscular related factors, rather than a single factor may be implicated in the osteoarthritic disease process.

Authors	Sample	Key Findings
Amara et al. [33]	41 cases with unilateral endstage hip OA	Muscle weakness on affected side may predispose the individual towards developing OA of contralateral hip
Bourne et al. [60]	42 rabbit patellofemoral joints	Repetitive, low intensity, prolonged developing OA of contralateral hip muscular loading raised vulnerability to injury
Christiansen et al. [76]	59 cases after knee arthroplasty	Weight bearing interlimb asymmetry of 0.69 one month post surgery was predicted by asymmetry in quadriceps and hamstring strength
Elboim-Gabyzon et al. [61]	60 cases with knee OA	Degree of fatigue was greater in leg that was less painful and rate of force development in contralateral leg was higher than affected leg
Fink et al. [9]	78 knee OA cases with end stage disease	VL muscle showed degenerative changes that correlated with the presence of a varus deviation of the leg
Grimaldi et al. [71]	12 cases with hip OA; 12 controls	Although subjects with mild degenerative hip OA were not significantly asymmetrical, those with advanced hip OA pathology demonstrated statistically significant asymmetry of the gluteus medius and piriformis muscles with smaller muscle volumes around the affected hip. This was consistent with gait patterns and OA stage
Hinman et al. [62]	89 hip OA cases;23 controls	Knee OA cases have excess hip muscle weakness unaffected joint muscles compared to controls
Lee et al. [63]	2839 Korean subjects with knee OA,	Sarcopenic obesity was more closely associated with OA than non sarcopenic obesity
Park et al. [64]	19 cases with TMJ OA; 20 controls,	Muscle fatigue was more readily seen in those with OA joint changes
Rasch et al. [72]	22 cases with unilateral hip OA	Major hip and knee muscles showed strength declines and muscle mass losses not fully explained by strength loss; infiltration of fat and other non contractile elements was substantial
Rearadon et al. [65]	12 post-operative hip OA surgery cases	There was significant quadriceps atrophy and type 2A and 2B muscle degeneration 5 days after surgery; the atrophy of all fibers persisted at 5 months despite exercise intervention
Rutherford et al. [66]	20 unilateral symptomatic hip OA;20 controls	Bilateral knee mechanics suggestive of muscle fatigue were found in the OA group that were symptomatic
Rutherford et al. [67]	20 hip OA cases; 20 controls	Knee muscle activation patterns differed from controls-and appeared to be more fatigue susceptible Both knees showed activation changes
Sanchez-Ramirez et al. [68]	285 knee OA cases	Inflammation might influence muscle strength in OA
Shanahan et al. [69]	30 knee OA cases;30 controls	Knee OA cases had worse triceps surae postural responses than controls
Tanagushi et al. [70]	21 women with knee OA, 23 without	Muscles of the OA group were not the same as healthy group, and differed within the subject within the OA subjects in terms of muscle thickness measured by US
Terracciano et al. [72]	15 women with OA; 15 with osteoporosis	Muscle atrophy of both fiber types occurs to same degree and is related to the functional impairment associated with the disease. This is not the same for cases with osteoporosis
Thorlund et al. [59]	22 cases at risk for knee OA	Differences in muscle strength after partial meniscectomy may predispose to knee OA
Vahtrick et al. [13]	12 women with knee OA pre/post surgery	No post surgical changes in voluntary activation and rapid contraction and relaxation capacity was observed at 3 and 6 months
Valente et al. [75]	Used a generic musculoskeletal model to healthy Subjects	Gluteus medius weakness affects joint contact forces at hip and ankle, but more so at the knee joint that may affect OA onset/progression
Zeni et al. [18]	56 hip OA cases prior to surgery	Knee extensor and hip abductor strength predicated function and strength was asymmetrical from side to side; or between 26-28% lower on affected side.

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Abnormal muscle activation [23, 29, 43, 55]  
 Cyclic sub-maximal muscle loading [4]  
 Muscle afferents [24]  
 Muscle agonist:antagonist force ratios [76]  
 Muscle composition [85]  
 Muscle contractures  
 Muscle contractile properties  
 Muscle coordination [67]  
 Muscle cross sectional areas [23, 70]  
 Muscle endurance [13]  
 Muscle fatigue [61, 64, 66]  
 Muscle fiber atrophy [33, 47, 65, 72]  
 Muscle fiber:fat ratio [44, 63]  
 Muscle inhibition [13]  
 Muscle inflammation [68]  
 Muscle injury  
 Muscle metabolism  
 Muscle morphology [9]  
 Muscle pain  
 Muscle paralysis  
 Muscle strength [13, 72, 75, 84]  
 Muscle rate of force development [13, 23]  
 Muscle volume [71, 72, 83, 85]

**Box 1:** Possible neuromuscular pathways and physiological attributes that could impact osteoarthritis disease processes?

Biopsy [72]  
 Computer Assisted Tomography [38]  
 Electromyography [6, 23, 81]  
 Force plate analysis  
 Functional magnetic resonance imaging [74]  
 Gait analysis [79]  
 Immunochemistry  
 Isokinetic dynamometry [79]  
 Magnetic Resonance Imaging [38, 71, 83]  
 Mathematic models [75]  
 Mechanical vibration [69]  
 Muscle activation and co-activation [13, 23]  
 Muscle composition [85]  
 Muscle endurance  
 Muscle fiber analysis [9, 33]  
 Muscle quality-a measure of muscle strength per unit size  
 Muscle biochemistry tests  
 Muscle rate of force development [23, 79]  
 Muscle strength capacity [22, 59, 65, 72, 77, 84]  
 Nerve conduction tests  
 Proprioception [82]  
 Radiological density of muscle [72]  
 Twitch interpolation technique [14]  
 Ultrasound [38, 65, 85]  
 Vertical ground reaction force [76]

**Box 2:** Possible tools and types of tests that could be applied to evaluate pre and/or post-arthritis muscle function.

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