

Muscle and Osteoarthritis Joint Status: Current Research Highlights and Their Implications

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Abstract

Osteoarthritis, a disabling disease, commonly believed to originate in the articular cartilage of freely moving joints, affects the entire joint, including muscle. This brief highlights the current research being published in this respect, an area of research that is not well documented when compared to related studies of cell biology, tissue engineering, and molecular in vitro studies, among others. To this end, to update a prior analysis, PUBMED, and Web of Science indices were searched for information specifically published between Jan 2015 and April 2017) using the key words: Osteoarthritis and Muscle, among others. Results show, a reasonable body of current science based evidence continues to focus on one or more aspects of muscle structure and/or function in the context of furthering our understanding of the pathogenesis of osteoarthritis disability. Second, while not conclusive, a variety of changes in muscle quality, function, and/or estimates of muscle bulk appear to correlate temporally with features of the pathological processes and extent of disability. Third, well designed carefully construed treatments directed towards improving muscle structure and function in those with symptomatic osteoarthritis appear to hold more promise than not for potentiating favorable disease outcomes. Conversely, failure to identify what component of the muscle system is specifically implicated in the osteoarthritis disease process may produce more negative clinical outcomes than not.

Introduction

In 2017, Chen, et al. [1] affirmed the importance of all synovial joint structures, rather than simply the articular cartilage lining when discussing the pathogenesis of the painful disabling joint disease known as osteoarthritis. Another body of research shows acceptance of muscle strength as a factor in the osteoarthritic disease process [2,3], and that muscle dysfunction may be a causative or pre existing, rather than a reactive disease factor [4]. This brief expands this topic by examining recently published findings concerning quantitative and qualitative muscular changes observed in the context of the pathogenesis of osteoarthritic joint damage, given that a better understanding of the role of muscle in this condition may be extremely helpful clinically. Second, it stresses what researchers might focus on in the future, as well as what clinicians might do to ameliorate their client's osteoarthritis symptoms. This information was sought in a continuing effort to improve upon prevailing preventive options for countering osteoarthritis, the most prevalent joint disorder, and the leading cause of chronic joint pain and functional disability throughout the world.

In addition, it was specifically sought because the possibility that pathology of the neuromotor system, as well as excess or abnormal muscle forces may promote or exacerbate joint dysfunction may enable more targeted treatments for patients to emerge than are presently available. Moreover, the available literature housing multitudes of osteoarthritis related studies on articular tissue biology, pharmacologic and surgical options for osteoarthritis, stem cell research and tissue bioengineering, shows none have proven viable to date as either a treatment approach or conceptual framework for guiding clinical practice.

To examine the extent to which muscle appears to be implicated in the disabling and prevalent pathology of osteoarthritis, recent publications on this topic area were sought and carefully examined and analyzed.

Methods and Procedures

To examine the degree to which current research focuses specifically on muscle in the context of osteoarthritis, data embedded in peer reviewed English language publications containing the key words, osteoarthritis and muscle, and others, based on prior work in this realm were sought. The time periods covered were largely limited to those publications reported between June 2015 and April 2017, given available prior comprehensive analyses on this topic [eg. 5-8]. Data bases employed were: PUBMED and Web of Science. Results were limited to clinical non-experimental studies that assessed some form of muscle quality or structural property in the context of osteoarthritis. Excluded were animal models, as an appropriate replicable animal model of osteoarthritis and relevant muscle

Table 1: Extent of possible current sources of information on muscle and osteoarthritis.

Data Source	Key Words and Number of Citations
PubMed Jan 2015-April 15, 2017	Muscles and osteoarthritis-535 Knee osteoarthritis and muscle-404 Hip osteoarthritis and muscle-153 Hand osteoarthritis and muscle-40 Muscle abnormalities in osteoarthritis-39 Muscle atrophy and osteoarthritis-41 Osteoarthritis and muscle pathology-86 Motor control and osteoarthritis-46 Sarcopenia and osteoarthritis-27 Muscles and their role in osteoarthritis -20
Web Science Jan 2015-April 15, 2017 [5 data bases]	Muscles and osteoarthritis-1601 Knee osteoarthritis and muscle-925 Hip osteoarthritis and muscle-372 Hand osteoarthritis and muscle-86 Muscle abnormalities in osteoarthritis-37 Muscle atrophy and osteoarthritis-31 Osteoarthritis and muscle pathology-679 Motor control and osteoarthritis-116 Sarcopenia and osteoarthritis-31 Muscles and their role in osteoarthritis -14

problem has not yet been agreed upon. Abstracts were deemed acceptable if published in English, and all forms of osteoarthritis were considered. Only a narrative summary and descriptive analysis was possible.

Key Findings

Despite a sizeable number of possible thematic related publications identified at PUBMED and Web of Science data bases over the past two years, only a limited number were found to specifically focus on the present topic of interest [see Table 1 for various key words used and their yield].

Among these publications, most were derived from cross-sectional studies, studies based on mathematical modeling, or prospective studies of post surgical patients. Rather than any coherent body of information, these publications included a very broad array of thematic topics, rather than any uniform body of content. These topics included observations of how various forms of muscle dysfunction interact with various forms of osteoarthritis pathology, various measures of osteoarthritis pain, and various aspects of osteoarthritis function [9-11]. Others described the relationship between muscle contraction durations [12], or the rates at which selected muscles contract [13] and their association with the extent of the prevailing osteoarthritis pathology [eg. 14,15].

Yet others focused on examining the association between the impact of muscle co-activation processes on joint moments [16,17], sarcopenia and its relationship with osteoarthritis [18], muscle activation imbalances [19], the role of abnormal muscle loading forces [20], and muscle weakness and movement patterns [21] in the context of osteoarthritis.

Additional themes focused on possible the relationship of osteoarthritis to muscle structural abnormalities, muscle mass alterations [22], motor control abnormalities, altered muscle co-activation patterns [23], and muscle thickness abnormalities [24]. Other themes focused on muscle strength and inflammation [25-26], and aspects of muscle power and function [27,28] in the context of various forms and degrees of osteoarthritis.

Other topics housed in the current literature focused on the impact of skeletal muscle vitamin D levels on osteoarthritic muscle [29, 30], the role of muscle imbalances in osteoarthritis [31], and the role of atrophy of distant muscles as a significant correlate of osteoarthritis [32]. The role of muscle composition changes, muscle fat infiltration [33], and negative contractile changes and its impact on osteoarthritis was also discussed [34].

To add to the diversity of this information, almost all studies employed different assessment approaches, even if a similar variable or idea was examined. In addition, some reported associations between reduced rates of torque development and intrinsic contractile deficits [14], while others noted an association between having a proportionately lower lean body (muscle) mass and osteoarthritis [35-36]. Another body of current literature focused on the role of muscle thickness, the role of altered moving distance of the muscle insertion, and the role of mental health in mediating or moderating osteoarthritis strength and disability [37,38].

While many studies of osteoarthritis have examined muscle strength capacity and its outcome at various joints, most conclusions are based on the role of concentric strength measures, rather than eccentric strength measures. However, consistent with Serrao, et al. [39]. Petrella, et al. concluded a reduced ability to generate eccentric muscle forces in a timely manner [40] is a more significant factor in terms of explaining cartilage damage than concentric strength values. Yet, others have stressed the importance of abnormal dynamic muscular force adaptations [41-43], afferent sensory dysfunction [44,45], dysfunction of the tendon-aponeurosis entity of muscle [46], along with diminished strength capacity [47], co-ordination impairments, co-activation ratios and sums [17] in explaining the osteoarthritic pain and disability cycle. Alternately, others imply it is reduced muscle endurance, rather than muscle strength that influences joint force abnormalities associated with the disease process [48].

In this regard, Astephen-Wilson, et al. [49] found cases with knee osteoarthritis do experience abnormal loads of their major weight bearing joints bilaterally, and these abnormalities persist despite treatment of the affected limb. However, whether these findings are attributable to the presence of either pre existing muscle pathology and /or an alteration in afferent input to the central nervous system and long term adaptations that may prove detrimental to articular cartilage in vulnerable joints such as the knee is impossible to establish. Although Ferrari, et al. [50] found concomitantly worsening of the muscular deficit and atrophy of hamstrings led to persistent and disabling knee pain associated with osteoarthritic joint damage, in a patient with progressive amyotrophy, whether this occurs in osteoarthritis cases more generally over time is also not known.

Nonetheless, Tuna, et al. [51], and Macias-Hernandez, et al. [52] reported finding early changes in femoral, tibial, and patellar cartilage that were significantly correlated with muscle strength, and suggested these early changes might play an important role in the pre-clinical phases of osteoarthritis. Others state muscle associated changes observed in osteoarthritis are compensatory rather than causative [22,53], and that muscle power of the agonists as well as the antagonists on both the affected osteoarthritic limb as well as the contralateral limb affect temporal aspects of day to day function [27].

Colgan, et al. [54] who studied patients prospectively, noted that despite clinical score improvements for pain and functional ability

post surgery, this did not translate to the expected degree of dynamic gait improvement. They indicated that post-operative rehabilitation programs should include extensor muscle exercises to increase power and to retain the operative gain in passive range of motion, which might help improve gait patterns. This idea was supported by findings that lower limb muscle activation patterns do appear to be significantly altered for four of the lower limb muscles of the affected limb of the osteoarthritis limb during stair climbing. These adaptations were said to be indicative of co contraction strategies in the total knee arthroplasty patient [55], but could have been related to changes in muscle composition of multiple muscles, rather than function alone [33].

or duration, or muscle balance or muscle power or some other muscle attribute should be examined, and if so, in what way-clearly precludes any meaningful synthesis of this research. Moreover, even with prospective analyses, which are more supportive of a temporal relationship of the muscle and joint disturbances, attempts to isolate sub categories of muscle dysfunction for purposes of a systematic analysis are extremely challenging at best, because key words selected to describe a specific topic, do not always comport with or yield the desired data. As well, which if any of the muscle function assays represent protective reactions, rather than pathological correlates or adaptations, is also impossible to discern with any clarity at the present time? (Table 2).

Table 2: Random sample of diverse topics focused on in current literature concerning muscle and osteoarthritis over time periods Jan 2015-April 2017.

Research group	Joint	Muscle Attribute	Observation
Bamman et al. [25]	Hip	Muscle inflammation, protein syn.	Muscle inflammation and suppressed muscle protein synthesis was evident in non traumatic total hip arthroplasty patients affected limb
Culvenor et al. [14]	Knee	Knee flexor + extensor strength	Thigh strength predicts risk for knee replacement in women
Harding et al. [58]	Knee	Knee + ankle muscle forces	Obesity increased posterior muscle forces and joint forces during gait, which may exceed joint ability of OA cases to accommodate load readily
Hodges et al [12]	Knee	Co-contraction duration knee	Augmented knee muscle co contraction speeds up medial compartment knee OA progression
Jeong et al. [59]	Knee	Surface electromyography	Flexion-relaxation rates of erector spinae was not the same in older osteoarthritis cases as in younger cases
Lee et al. [48]	Knee	Ratio leg muscles/fat mass	Leg muscle mass correlates with pain
Omori et al. [60]	Knee	Quadriceps strength	Dynamic quadriceps strength is likely to be more strongly associated with radiographic grade of knee OA than static measures
Petrella et al. [40]	Knee	Muscle strength	Lower knee extensor torque is associated with pain, stiffness, and function
Takacs et al. [61]	Knee	Concentric/eccentric knee strength	Decreased muscle strength and frontal plane stability during external perturbation and reduced proprioception appeared related
Tsukagoshi et al. [62]	Hip	Peak hip extension angle + muscle weakness	Peak hip extension angle correlated with hip and knee muscle strength, and peak hip extension angle during gait
Wakabayashi [63]	Hip	Muscle mass	Preoperative psoas muscle mass on non operative side was associated with postoperative gait speed mass
Zacharias et al. [34]	Hip	Hip abductor muscle volume	Gluteal muscle atrophy and fat deposits were related to disease severity

*Prospective study

OA=osteoarthritis; syn=synthesis

In sum, in concordance with prior work on the present topic, it appears that alone or in combination, muscle structure and/or function or both are often found impaired or altered in some way among adults with varying degrees of osteoarthritis. These impairments are frequently distinctive from age associated changes or deficits, regardless of pain or radiographic changes [57], and may predate, as well as exacerbate osteoarthritic pain and dysfunction quite significantly and in a dose dependant manner, even if this finding is not universal [58]. Muscle impairments can also influence functional status significantly, regardless of joint status, along with surgical efforts to relieve pain [54]. In turn, joint impairments can selectively impact muscle quality, quantity, and function.

As outlined in Table 2, these muscle impairments, which may differ among muscles of the same individual, have been observed at early stages of the disease, as well as later stages [24]. These abnormalities or adaptations may include, but are not limited to, a wide variety of strength and motor control deficits, alterations in muscle structure, alterations in the temporal characteristics of local and distant muscles, along with alterations in muscle proprioception and muscle fat content. However, which are of greatest importance in terms of impacting the different phases of the osteoarthritic disease process at different joints is currently impossible to discern with any clarity. Indeed, the lack of uniformity in cohorts studied, unknown effects of age, weight, and comorbid disease on muscle function and structure among these cohorts, differing research designs, along with confusion as to whether muscle strength, cocontraction magnitude

Discussion

Evidence that muscle is involved in the osteoarthritic process is increasing steadily, along with the possibility that muscle weakness, muscle balance [31], muscle power deficits [64,65], low skeletal muscle mass [66], and disturbances residing in the neuromotor system may be a causative, rather than a reactive disease factor [44,51,67,68]. Supporting this idea are findings that those with stronger muscles may function more ably than those with weaker muscles [43,69], while those with symptomatic osteoarthritis show different muscle activation patterns than those generated by asymptomatic individuals with the same radiographic grade [49], which could influence skeletal cell behavior [70]. They may also experience less pain as well as better function [15,66,71] and better joint stability over time [44].

However, even where muscle is observed to be implicated in the pathogenic process, it is not possible at present to establish which muscles are of most import in mediating or moderating various forms of osteoarthritis. Support for any causative role for muscle in the osteoarthritic disease process is especially challenging given that most studies embracing this topic remain cross-sectional without any consistent conceptual model or set of consistent hypotheses. Unsurprisingly, whether muscle power rather than strength is potentially highly important in mediating the disease [64,65,72], or whether muscle timing, muscle mass, muscle co-ordination, muscle co-contraction, muscle fatigue, or imbalances are paramount in this

disease process, is impossible to discern with any clarity. Gender, weight status, nutritional status, general health status, trauma and aging factors and their influence on either muscle or joint status or both are also extremely difficult to tease out with so few well designed and adequately powered predictive studies.

Hence, despite a reasonable volume of research directed towards assisting practitioners and researchers to better understand this topic, no apparent conclusions about a definitive role for any aspect of muscle structure or function or both in the osteoarthritis pathogenic process can be forged. As a result the clinical implications of this body of knowledge are unclear at best.

That is, despite a reasonably vast array of related studies on this present topic, related current studies seem to have few commonalities or guiding principles to rationalize their objectives and approaches. Not only are different disease stages studied, with different tools, and with dissimilar premises and aims, but the challenges in synthesizing data from morphological studies, [39,46], alongside electromyographic studies [eg. 19,53,59], muscle volume studies [36], plus studies examining the role of elevated skeletal muscle FoxO1 protein and reduced IL-15 protein expression and strength in people predominantly with knee osteoarthritis [26], remains immense.

In addition, even though the impact of muscle weakness on pain or radiographic changes [56], appears to be a consistent finding across several studies, the relative importance of muscle strength versus other muscle attributes, and their possible temporal order of development, is unclear in the absence of comparative and prospective evaluations of other muscle attributes. These include muscle endurance, muscle fatigue, muscle imbalance, muscle inflammation and abnormal muscle fat content [74].

Similarly, not all authors agree on the relevance of muscle impairments in the context of osteoarthritis, even when examining similar issues. Farrokhi, et al. [73] for example, found contact mechanics in cases with knee osteoarthritis to be unrelated with muscle strength mechanics, while others have implied there is a relationship between knee flexor moments and pain at the osteoarthritic knee [75]. As well, Skou, et al. [57] found muscle strength was not a predictor of an increased risk for knee replacement, even though others found that changes in neuromuscular function can conceivably predate the disease onset [44,71] and can strongly predict pain and extent of disease [22,60].

In another report, Lim, et al. [76] found no trend to exist between measures of quadriceps electromyography and knee alignment in people with knee osteoarthritis, even though subjects who were less impaired had similar muscle patterns to those who were severely impaired, and the presence of imbalanced vastus medialis, lateralis ratio was not equitable from within subjects. However, the sample size was small, ages studied were younger than 60 years of age, and body mass on average was in the normal range, while the torque measures were examined during seated contractions, not weight bearing positions.

In addition, concentric strength may be less important than eccentric strength in men [39], muscle strength may predict disease progression for women, but not men [14], endurance may be highly important, not strength [48], and muscle fat content may be more important than not [74]. As well, as shown in Table

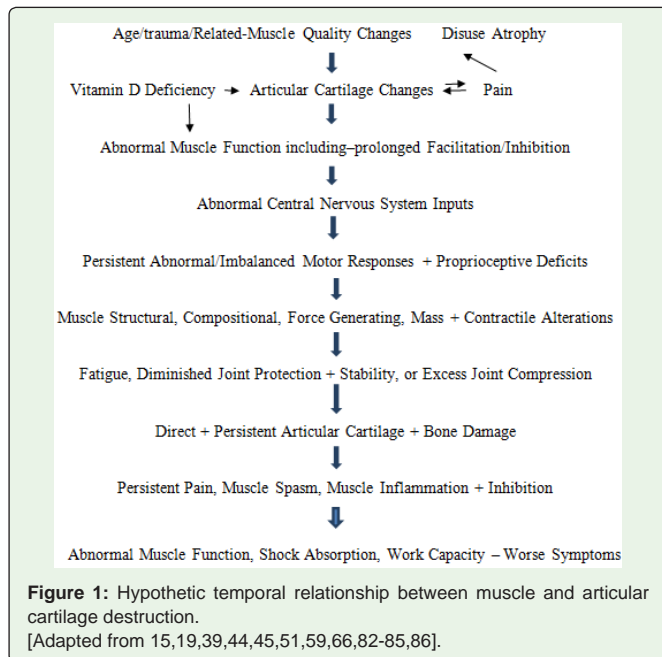
2, data representing this topic stem largely from studies of knee or hip osteoarthritis, but are poorly articulated for joints other than the hip or knee, even though osteoarthritis of the hand, neck, back, ankle, elbow, and shoulder are all sites that produce severe disability. Surprisingly, very few studies have examined osteoarthritis cases with multiple joint involvement even though this is more common than not and could be very telling.

As well, the use of data from intervention studies, where control subjects could still sustain an 'intervention' effect [12], differences in self-reported function [77,78] versus actual function [79], differences in the nature of the functional activities assessed, plus differences in muscle measurement tools, joints, muscles and muscle attributes examined, along with disease status differences, severely limit the ability to extract any conclusive trends of import from this data. Moreover, though discrepancies between muscle power versus strength prevail, the actual impact of muscle power on joint physiology and structure is not well described, when compared to the correlate of strength [51].

In short, despite more than 40 years of efforts to examine muscle status in the context of osteoarthritis pathology, no firm conclusion about its etiological role, nor what aspect of muscle status or impairment is most salient - if indeed a temporal association, prevails. While it is recognized some relevant research may not have been located, or has been published in former years, or in a foreign language, the role of muscle as a protective factor in minimizing joint forces and impact as indicated by Bouchouras, et al. [53], along with the possibility that rather than muscle being a compensatory or reactionary joint component, excessive muscle co-contraction found in osteoarthritis may be a maladaptive response [86], has also not received wide examination when compared to other aspects of osteoarthritis pathology. However, regardless of these limitations, and the fact negative studies may not be published, it seems possible that by drawing on the prevailing data base, those in the field can be encouraged to work together to develop a more universal conceptual model of how muscle adaptations and joint status may be interrelated in the osteoarthritic disease process [see Figure 1 for a tentative set of ideas]. In particular, exploring whether different clinical profiles exist and whether tailoring interventions accordingly may foster the ability to deliver more personalized healthcare to this population warrants careful consideration [47].

Implications and Conclusion

While harnessing the entire data base to systematize more definitive trends than is evident in the present snapshot of current research may be valuable, it is the author's belief that more efforts towards developing carefully construed biomechanical, radiological, molecular, biochemical, and neuromuscular oriented prospective studies of adequate duration are indicated to advance this line of inquiry, despite the increasing volume of reports. To verify or dispute hypothetical evidence based associations depicted in Figure 1 and expand upon trends depicted in Table 2, more prospective studies focusing on muscle co-activation effects [17], the role of eccentric as well as concentric forces on the emergence and progression of osteoarthritic joint disease [40], as well as the role of distant muscles [42,69], and the tendon-aponeurosis complex [46] are indicated [46,59]. In addition, delineating the role of muscle fat infiltration [33,81], muscle inflammation [25], and vitamin D [30] and its impact on muscle structure and function in the context of osteoarthritis may



prove exceptionally insightful [80], as may efforts to conduct well designed case control studies using validated instruments.

However, without a strong coordinated national or international task force to guide this line of research, it is probable that many laudable studies conducted to date in isolation may still prevent the emergence of any universal understanding or directive for advancing care. As well, without an agreement upon a standardized test battery for measuring the most important muscle attributes deemed salient in osteoarthritis on a routine basis, clinicians may fail to appreciate the important role played by muscle in osteoarthritis disease process, and how to use this information to directly foster optimal osteoarthritis outcomes.

Until more research is forthcoming though, the literature indicates clinicians should be encouraged to routinely examine the muscular as well as the joint status of their osteoarthritis clients, and to tailor their treatment recommendations appropriately. Indeed, regardless of joint status, employing this approach sooner, rather than later, and following up their initial findings with carefully construed targeted solutions known to impact neuromuscular function favorably, patients seeking to improve their joint status can expect to reap more benefit than not from such therapy, at all stages of the disease process.

Recommendations must clearly be applicable and commensurate however with the nature of the resultant and presiding interactions between the patients' muscles and joints, and what is considered beneficial in the individual situation, as well as harmful. Current literature is important to employ in this regard, given the fact that it houses general observations, as well as some unique findings that could help to reduce the disease burden, while modifying the disease process favorably. However, more research directed towards revealing the extent to which deficiencies in the motor system contribute to articular cartilage degeneration, and in what way, will most assuredly improve the prognosis for those at risk as well as for those with different degrees of osteoarthritis disability significantly, as well as profoundly.

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