

Muscle Function during Selected Weight-Bearing Activities in Adults with Knee Osteoarthritis- A Narrative Overview

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ABSTRACT

AIM: Osteoarthritis, a highly disabling long-term health condition is often resistant to standard treatment approaches focused solely on pain relief. Potentially implicated as a factor in the disease process, muscle is often a recommended target for intervention to alleviate the disability. How much research has been conducted to support the role of muscle in the disease process? Are muscular responses during functional tasks altered among adults with knee joint osteoarthritis? Can a case be made for an association between muscle dysfunction during functional tasks and osteoarthritic joint damage at the knee?

METHODS: Reports from major data bases aligned with this topic and extending from 1950-2016, were first examined to ascertain the extent to which muscle appears to have been examined as a potentially important correlate of knee joint osteoarthritis disability, in general. Data detailing muscle responses during weight-bearing tasks among knee osteoarthritis cases were then specifically examined. A narrative report was generated in light of the lack of any consistency in the available studies.

RESULTS: There is a substantive literature that has focused on muscle structural and function and their relationship to osteoarthritis disability, but most studies did not examine muscle function relative to functional weight-bearing activities. Among the latter, while there is some consensus that muscles around the osteoarthritic knee function differently in some cases from those of the healthy knee, it

is not clear whether this alteration is protective or pathological.

CONCLUSION: There is an increasing volume of literature detailing experimental observations of a linkage between muscle and aspects of function in adults diagnosed as having knee osteoarthritis. Most available research studies examining the impact of muscle associated interventions on the functional outcomes show some association, but this is not universal. Treating muscle in cases of knee osteoarthritis does appear to produce more favorable outcomes than not in this cohort. However, what accounts for this latter observation and what aspects of muscle dysfunction should be targeted for improving functional weight-bearing activities optimally is very hard to discern due to the diversity of related study approaches. Efforts to drive more efficacious treatment and preventive practices for the knee osteoarthritis population appear to clearly require some unifying hypothesis or framework to guide the desired research needed to elucidate the connection between muscle dysfunction and functional performance of the knee osteoarthritis patient.

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Key words: Functional Activity; Gait; Knee Joint; Muscle; Osteoarthritis; Pathology; Treatment

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INTRODUCTION

Osteoarthritis, a widespread chronic degenerative disorder of one or more joints, produces a high degree of disability, especially at the knee joint. A disease with no clearly defined cause and very few successful treatment options, including medications, and on occasion surgical interventions, current findings point to osteoarthritis as a disease of the whole joint, rather than solely the articular cartilage, the tissue of prime concern^[1]. Accordingly, Egloff *et al*^[2] suggested teasing out the independent role of muscles, tendons, ligaments, synovium, and bone in the biomechanical pathway to osteoarthritis

damage, may be especially helpful in this regard.

In this respect, there is reasonable evidence that osteoarthritis may arise as a result of imbalances between mechanical stresses placed on a joint and the ability of the joint to withstand these stresses^[3]. From this perspective, joint damage may consequently be specifically promoted if the muscles themselves are dysfunctional or abnormally affected in some way. For example, abnormal physical stresses can arguably be placed on the joint as a result of reactive muscle inhibition consequent to injury^[4], muscle weakness, uncoordinated muscular forces^[4,5] excessive muscular forces^[6-8], muscle atrophy, contractile dysfunction^[9], or all of these in combination^[10-12]. Moreover, in addition to one or more joints being adversely affected by a variety of reactive structural and functional abnormalities, muscles alone can arguably influence the onset of the condition, as well as outcomes of attempts to treat osteoarthritis significantly and negatively if they fail to absorb joint loads in a timely and optimal manner^[12,13].

Since improvements in the prevention and treatment of osteoarthritis depend on a clear understanding of its etiology, this review specifically sought to examine the extent to which the role of muscle dysfunction, potentially amenable to detection, classification, and intervention, has been examined in the context of knee joint osteoarthritis. A second aim was to examine which forms of muscle dysfunction might be the most salient to evaluate and address in future efforts to reduce the disease severity in the clinical setting. In this respect, this review examined the relationship between selected aspects of muscle function and functional activities among this patient group.

METHODS

To obtain the data desired for this overview and review, Web of Science and PUBMED data bases were searched using the terms *muscle and osteoarthritis*, *muscle and knee osteoarthritis*, *muscle dysfunction and knee osteoarthritis*. Only articles directly describing some type of muscle assessment and also measuring some aspect of weight bearing function were deemed acceptable for in depth review. It was hypothesized that research on muscles and their relationship to knee osteoarthritis pathology would be quite numerous and increasing in importance. It was also expected that the literature would be very diverse and contain a variety of seemingly unconnected findings, rather than any specific viewpoint as this line of discovery is still in its infancy if compared to general osteoarthritis studies that focus on articular cartilage, bone, and inflammation. To limit the array of factors that would make conclusions challenging, only data obtained in the context of non-surgical situations were considered, as joint replacement surgery involves cutting of muscle, and could thus be an unrecognized confounder variable. The articles selected for this commentary were only deemed acceptable for the present purposes if they included some type of functional measure and tried to establish the extent of any reported muscle dysfunction relative to the subject's functional ability. Other studies that assessed muscle function without testing actual function, and those that only assessed subjectively perceived disability were excluded.

RESULTS

General findings

In terms of our first aim, it was noted that regardless of data source, a considerable number of research publications examining the topic of muscle in the context of osteoarthritic disease process have been

forthcoming over the past several decades. Moreover, this line of research has continued to increase in size over the past five years as outlined in the summary table below.

In terms of our second aim, we noted that among these data, there were many divergent themes, various samples and types of osteoarthritis studied, various stages of the disease, different study designs and follow up periods, various methods of assessing muscle structure or function prevailed, when this was documented, and some studies focused on muscle as a disease precursor, while others focused on muscles as a reactive pathogenic factor (See Figure 1). In fact, this cursory analysis revealed a very broad spectrum of muscular mechanisms possibly involved in the osteoarthritis-disability cycle, including: muscle strength deficits^[14,15], abnormal muscle activation patterns^[16], abnormal muscle loading forces^[17], proprioception problems^[18], muscle inflammation^[19], deficits in muscle rate of torque development^[20], abnormally coordinated muscle function^[21] muscle structural abnormalities^[22], muscle flexor/extensor imbalances^[23], and problems attributed to impaired muscle afferent activity^[24]. To discern if any of these factors are associated with functional activities of daily living, and if so in what way, only studies that examined muscle function in the context of functional activities in knee osteoarthritis cohorts who had no surgical history were examined. In terms of ordering the data, no specific chronology was used, but it was hypothesized among the available studies, knee muscle co-ordination problems, rather than knee muscle strength deficits would be strongly related to one or more aspects of functional mobility.

Specific findings

In terms of establishing if muscle force generation processes are implicated in the etiology of knee osteoarthritis, the key observation from the studies presently retrieved and fulfilling the review criteria was the immense heterogeneity of muscles studied, modes of analysis, movements examined, disease presentation, and control samples employed. For example, that by Lee *et al*^[31] examined a cohort comprising 35 patients with unilateral medial osteoarthritis and varus deformity where it was reported that the total work of the quadriceps ($r = 0.429$, $P = 0.037$) and hamstring ($r = 0.426$, $P = 0.045$) muscles at 180°/sec each correlated with the magnitude of the knee adduction moment. It was further reported that quadriceps endurance at 180°/sec was the only factor independently associated with adduction moment ($\beta = 0.790$, $P = 0.032$), and not strength, quite well-established disease correlate. However, as outlined by Shull *et al*^[32] the underlying muscle force modifications that appear to impact knee osteoarthritis gait patterns may be quite complex, and it is not clear how the ability to generate more muscular work or how having more muscular endurance produces more observable joint loading according to the direction of the correlations uncovered. This would mean that subjects with better test scores recorded on a dynamometer are possibly at greater risk, rather than a lower risk of medial compartment loading, or that those who have greater alignment problems, and a higher need to protect the medial compartment during gait develop more proficient muscle function as suggested by Lim *et al*^[37]. The muscle measures were also conducted in a non-functional position that is not employed during actual functional tasks, and only one velocity parameter was measured, even though rate of muscular contraction during functional activities such as walking are likely to be performed at lower velocities or varied velocities.

In this regard, Metcalfe *et al*^[33] found patients with knee osteoarthritis experienced abnormal loads of their major weight

Alignment and muscle action in knee osteoarthritis^[36]
 Differences in muscle activity between cases with osteoarthritis and healthy cases^[7,34,78]
 Hamstring-quadriceps muscle balance in knee osteoarthritis^[9,65]
 Impact of cyclic concentric and eccentric submaximal muscle loading^[5]
 Interlimb symmetry and co-contraction in knee osteoarthritis^[61]
 Knee muscle activation during sit-to-stand in knee osteoarthritis^[26,43,86]
 Knee muscle activation during walking^[35,39,41,57,60,64,69,72,73,74,75]
 Knee extensor power and mobility in knee osteoarthritis^[30]
 Morphological changes in vastus medialis in knee osteoarthritis^[10,22]
 Motor unit properties in knee osteoarthritis^[49]
 Motor control/dysfunction in knee osteoarthritis^[25,37,54]
 Muscle afferent neurons and osteoarthritis^[24]
 Muscle contractile deficits^[9,20,85]
 Muscle cross-sectional areas and knee abnormalities^[23]
 Muscle inflammation and walking^[19,27]
 Muscle strength and inflammation in knee osteoarthritis in older women^[81]
 Muscle strength and proprioception^[18]
 Neuromuscular adaptations during stepping^[16]
 Neuromuscular stabilization in knee osteoarthritis^[12]
 Obesity and knee muscle function in knee osteoarthritis^[76,83]
 Quadriceps endurance and knee adduction^[31]
 Quadriceps fatigue in knee osteoarthritis^[77]
 Quadriceps function before and after knee arthroplasty^[13]
 Quadriceps rate of force development in knee osteoarthritis^[29,55]
 Quadriceps strength and radiographic knee osteoarthritis^[14,51,53,84]
 Quadriceps power and knee mechanics in knee osteoarthritis^[42,66]
 Quadriceps activity during stair stepping in knee osteoarthritis^[59,62]
 Submaximal force steadiness and knee adduction moment in knee osteoarthritis^[80]
 Postural control and thigh muscle activity in men with knee osteoarthritis^[40,47]
 Role of muscles in joint adaptation and degeneration^[8,17]
 Vastus medialis fat infiltration and knee osteoarthritis^[48]

Figure 1 Broad array of muscle related topics covered in related literature.

bearing joints bilaterally, and these abnormalities persisted despite treatment of the affected limb. Not only were adduction moment impulses elevated at both knees and the contra-lateral hip compared to controls re-operatively, but co-contraction of hamstrings and quadriceps was elevated bilaterally as well. However, whether the abnormal loading was due to alterations in the rate of force development as well as the overall force, or both for the muscles assessed was not clear as the co-contraction parameter was calculated at 100 points through stance for the medial quadriceps and hamstrings and the lateral quadriceps and hamstrings separately, although this was later combined to represent overall outputs of each muscle. Controls and patients walked at self-selected speeds, but not necessarily at the same speed.

Cheing *et al.*^[37] reported that patients with knee joint degeneration had weaker quadriceps and hamstring muscles than controls, and that their knee range of motion of the affected leg was reduced by 11.2% and by 14.7% during walking. The relevance of these findings was not totally clear though, but compared to control subjects, the patients' walking speed was significantly slower. In early work by Messier *et al.*^[38], this group noted 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 significantly than if the muscles were well balanced and coordinated temporally and in magnitude since the muscles are important shock absorbers. The exposure of the cartilage to excess loading impacts that can produce cartilage damage, in turn can potentially produce reactive effects in the knee joint muscle structure and function that perpetuates the condition.

Mathematical modeling work by Brandon *et al.*^[39] suggests selective muscle activation forces of the lateral quadriceps and hamstring muscles, in conjunction with inhibition of the medial

gastrocnemius muscle during early stance could be a related factor to consider in the development of medial knee osteoarthritis. As well, the strength imbalance found between the knee flexors and extensors of an affected leg in the later stages of the disease or those imbalances within the muscle components alone^[40] may promote further wear of the already disrupted surface as indicated by a recent anatomical study of the relationship between focal osteoarthritic lesion sites on the femoral condyle of the severely damaged knee, which showed these coincided quite consistently with the magnitude and site of the prevailing flexion contractures and the degree of loss of knee extension. Muscle weakness or imbalances that may arise consequent to injury, may thus prove harmful to the physiology of the adjacent joints and others over time, if the muscle dysfunction is not corrected optimally. Hubley-Kozey *et al.*^[41] concluded that the magnitude of the co-activity measures assessed for four medial and lateral knee muscle pairs over initial stance was partially indicative of the severity of the prevailing knee osteoarthritis pathology.

Murray *et al.*^[42] however, argued that quadriceps power strongly influenced the knee adduction moment during gait, and recommended this parameter be assessed at a variety of loads to gain more insight into the nature of this relationship. Another parameter distinguishing the characteristics of the knee osteoarthritic patient from health controls is their greater degree of eccentric quadriceps/hamstring muscle co-activation during movements from an upright to a seated position^[43]. Davidson *et al.*^[43] found these movements were also performed more slowly than those of control subjects, and appeared to be protective, rather than pathological. Another study of the gait characteristics of patients with chronic osteoarthritis of the knee showed that along with gait deficits, subjects had less range of motion, and experienced more load moments at the knee, as well as prolonged rectus femoris activation^[44]. It was not clear if the rectus femoris activation duration was indicative of a protective strategy, but according to Alkjaer *et al.*^[25] who studied motor control and gait in people with knee osteoarthritis the soleus H-reflex amplitude, found to be higher at heelstrike than those of the controls, was hypothesized to represent a preparatory process employed to avoid sudden knee joint collapse that can occur in this disease. This may however vary, however, especially if there is knee joint effusion, which appears to modify knee mechanics during gait^[45]. See Table 1.

DISCUSSION

As shown in Table 2, many studies have focused on examining the possible linkages between muscle and the development and progression of osteoarthritis. As outlined in Table 1, which represents a reasonable cross section of recent studies in the specific realm of establishing the interaction between muscle and dynamic joint function in everyday tasks among adults with osteoarthritis, a wide array of study topics and approaches have clearly been applied. Among these, almost all case control studies show the measured muscular attribute in these studies commonly clearly differentiates those with and without the disease. However, the nature of these differences is often less than intuitive, and even when clearly described, often hard to interpret. For example, while some abnormalities appear compensatory^[25,26], or related to compromised frontal-plane joint stability, rather than strength^[46], other data show knee muscle strength and time at which submaximal force at the knee is generated to be strongly associated with knee joint power and function^[29], and possibly with joint loading and ultimate joint pathology. In addition, muscle endurance rather than strength may be a potent determinant of abnormal joint loading^[31].

Table 1 Selected studies suggesting a wide variety of muscle related abnormalities can be evidenced among cases diagnosed as having knee osteoarthritis when performing a variety of functional activities or in relation to functional activities.

Authors	Sample	Tool Used	Key Findings
Accettura <i>et al</i> ^[30]	55 cases	Strength and power	Knee extensor power was a good predictor of stair climbing and walking ability
Alkjaer <i>et al</i> ^[25]	11 females with OA 11 healthy controls	Soleus H-reflex amplitudes	OA group showed a trend to having a facilitated soleus H-reflex in swing-stance-transition phase of gait
Bouchouras <i>et al</i> ^[26]	11 women with OA 11 control women	Electromyography	Cases used greater degree of knee muscle co-contraction, + altered hamstring activation compared to controls during sit-stand activities, which may be protective
Cheing <i>et al</i> ^[37]	66 cases 10 controls	Isometric peak torque	Knee torques + gait velocity were compromised in patients
Childs <i>et al</i> ^[34]	24 unilateral cases 24 controls	Muscle activation during gait	Significant co-activation and duration increases were observed along with reduced peak vertical ground reaction forces relative to body weight
Davidson <i>et al</i> ^[43]	10 cases end stage OA 3 healthy control	Strength Electromyography	Patients had higher degrees of eccentric co-activation than controls
Hassan <i>et al</i> ^[47]	77 patients 63 controls	Postural sway	Patients had increases in postural sway, and quadriceps weakness
Lee <i>et al</i> ^[31]	35 knee varus OA cases	Knee strength + endurance	Knee adduction moment during correlated with quadriceps endurance at 180 degrees/s
Lyytinen <i>et al</i> ^[40]	54 men with OA 53 healthy men	Electromyography	Vastus medialis activity in patients was increased during a balance test, but balance was not compromised
Metcalfe <i>et al</i> ^[33]	20 cases unilateral OA 20 controls	Electromyography	Muscle activity during gait was increased bilaterally
Resende <i>et al</i> ^[46]	39 women with OA 39 controls	Joint power profiles	During gait, less energy was absorbed at the OA knee
Rutherford <i>et al</i> ^[35]	82 OA cases-3 groups 35 healthy controls	Electromyography	Alterations in muscle activation patterns, but not knee strength were observed in OA groups in terms of amplitude and temporal patterns from medial gastrocnemius and lateral quadriceps and hamstrings during gait that correlated with structural severity
Sanchez-Ramirez <i>et al</i> ^[27]	186 knee OA cases x 2 yr	Strength	Increased knee flexor strength was associated with better stair climbing in moving from sitting to standing
Shull <i>et al</i> ^[32]	10 medial knee OA cases	Toe in/out movement	No consistent pattern of muscle activation was observed
Tanaks <i>et al</i> ^[28]	52 cases with knee OA	Strength	Strength and dynamic balance were related
Winters <i>et al</i> ^[29]	26 cases with knee OA 23 healthy controls	Strength + rate force dev.	Quadriceps power was lower during fast walking in OA group, their maximal voluntary contraction predicted stair climbing time

Note: Bolded items refer to the muscle attribute of most significance.

Consequently, even though Rutherford *et al*^[35] concluded findings of muscle activation pattern differences consistent with systematic delays in temporal responses, represented an increased demand for active stiffness overall and in particular during mid-stance among cases with knee osteoarthritis of varying severity, and that decreased medial compartment joint loading throughout the stance phase is associated with increased structural severity, it is impossible to clearly discern what muscular correlates of knee osteoarthritis are pathological and which are protective. Furthermore, in light of the great variation of adaptive muscle activation patterns found among and within the muscles of adults with varying degrees of knee osteoarthritis, for example, the lateral knee muscle sites in one study were deemed reflective of the progression along the continuum from asymptomatic to severe osteoarthritis, whereas the medial muscle site measures differentiated severity between osteoarthritic groups^[41], it is presently impossible to outline or formulate any global theory about how muscles around the knee contribute directly or indirectly to knee joint osteoarthritis as outlined by Shull *et al*^[32]. In addition to the aforementioned observations, muscle power^[42], and eccentric rather than concentric muscle coactivation^[43], as well as pain and a variety of muscular abnormalities may accompany osteoarthritic joint damage^[47-50], and/or may independently or collectively heighten activity limitations and central nervous system responses that foster the development of the disease^[51-53], but these factors have not commonly been examined in the context of the studies reported here.

This is surprising given that subjects with knee osteoarthritis do present with significant muscle impairments that affect physical

function^[54] as well as wide variations in whole muscle contractile kinetics^[55]. Rate of force development^[13], and effusion, a determinant of muscle function in knee osteoarthritis, is also not well correlated with findings in the context of the present topic^[45].

Hence, although muscle strength is often a target of therapy for knee osteoarthritis, there is no direct information from current studies that this approach will be universally desirable or effective. Whether any muscular alterations should be deemed desirable is also unclear. Among the data that add to the confusion is that by Rutherford *et al*^[35] who noted no knee muscle strength differences among three groups of knee osteoarthritis cases, although features of medial gastrocnemius, lateral hamstring and quadriceps amplitude and temporal patterns differed among the groups. This did not align directly with the observations of Accettura *et al*^[30] who concluded that among adults with knee osteoarthritis, knee extensor power is a stronger determinant of walking and stair climbing performance than measures of knee extensor strength, but how having muscular power impacts knee medial compartment loading when compared to having lower levels was unclear. Hodges *et al*^[56] data in turn, support the hypothesis that it is augmented medial knee muscle co-contraction that underpins faster progression of medial knee osteoarthritis, while increased duration of lateral muscle co-contraction protects against medial compartment loss, even though Winby *et al*^[57] found more inconsistencies than not in the correlations between electromyographic measures of coactivation and articular loading^[57]. Hinman *et al*^[58] found individuals with knee osteoarthritis do display altered quadriceps function and knee joint kinematics when

Table 2 Summary of search strategy and publication numbers.

Data Source	Key Words and Number of Citations
PubMed 1980-	Muscle and knee osteoarthritis-1 585; 737 in last 5 years Muscle abnormalities in osteoarthritis-125; 39 in last 5 years Medial compartment knee osteoarthritis and muscle; 81, 35 in last 5 years Muscle dysfunction and knee osteoarthritis; 826, 389 in last 5 years Muscles and osteoarthritis; 3 180; 1 240 in last 5 years
Web Science 1950-	Muscle and knee osteoarthritis; 6 382 Muscle abnormalities in osteoarthritis; 262 Medial compartment knee osteoarthritis and muscle; 129 Muscle dysfunction and knee osteoarthritis; 107 Muscles and osteoarthritis; 13 280

descending stairs, but this activation pattern is not uniform across different groups of subjects with varying degrees of joint damage, or within a specific muscle group within a single case^[59].

In addition to joint effusion criteria^[45], patients may need to be classified according to extent of postural sway, which is related to quadriceps activation and strength^[47], and by disease severity, age, and degree of muscle inflammation-if present, as one or more of these factors may alter knee kinematics and lower extremity neuromuscular function and load distribution during gait in some way^[19,63-65,67,68]. Very little work has examined patients with valgus deformities and lateral versus medial knee compartment osteoarthritis, and these angular deformities are not always accounted for in the present array of gait studies listed in Table 2.

Confusion also reigns, because contrary to the hypothesis that muscle function is abnormal in knee osteoarthritis when compared to control healthy subjects, Kumar *et al*^[60] found people with knee osteoarthritis responded in a similar way to healthy people when exposed to perturbations during functional weightbearing activities. Likewise Collins *et al*^[61] found no significant differences in the stiffness between cases with symptomatic knee osteoarthritis and healthy subjects, even though there was a slight trend toward enhanced co-contraction in the osteoarthritic knees. Sanchez-Ramirez *et al*^[62] too reported that in the early stage of knee osteoarthritis the mechanisms involved in stepping down are not altered, although greater degrees of co-contraction can be observed in patients with more advanced disease. This suggested more inefficient use of the knee muscles in the more severely affected group, where considerably more self-reported instability was documented, but whether this inefficiency is a significant disease correlate is unclear.

Several other study findings too provide conflicting data. For example, although lower extremity neuromuscular function during walking is altered in severe knee osteoarthritis, regardless of walking velocity^[69], fast walking did not increase or change biomechanical differences between osteoarthritis and control groups according to Landry *et al*^[70]. Yet, according to Zeni and Higgenson^[71] the slower gait speeds observed in people with osteoarthritis are likely due to alterations in the neuromuscular response strategy of the lower extremity.

Al-Zahrani *et al*^[44] however, attributed gait abnormalities in knee osteoarthritis to instability during stance and found these cases generated more moments, rather than less at the knee compared to a control group. In other research, Likavainio *et al*^[72] who examined gait and muscle activation in men with osteoarthritis, and healthy controls found no group differences in skin mounted accelerometer readings during walking on level ground, and that maximal loading rate was higher bilaterally in controls. Although different muscle activation strategies during level walking and stair ambulation were observed, differences in ground reaction force parameters were only minor at constant gait speeds when groups were compared. This

group only assessed vastus medialis and biceps femoris activity, and thus the nature of any lateral muscle activation of the knee extensors, which may aid in stabilizing the external knee adduction moment^[73] was not assessed. However Heiden *et al*^[73] also reported that although kinematic alterations in knee osteoarthritis patients during gait do occur, these are not accompanied by alterations in knee joint moments. They also stated that larger adduction moments were related to lower-self perceived pain and symptoms, and lateral muscle activation which was higher in the osteoarthritis patient was correlated with the magnitude of the adduction moments. These findings are not consistent with the importance given to the vastus medial muscle and adduction moments as predictors of knee osteoarthritis damage, and results showing higher impacts during walking do occur in those with knee osteoarthritis when they adopt faster walking speeds^[74] and that subjects with moderate knee osteoarthritis increase the activity of the lateral sites and reduce activity or forces produced in the medial sites^[75].

CONCLUSION

The structure and function of muscles surrounding the knee, influential in the maintenance of normal joint structure and function, can be affected adversely by the osteoarthritic disease process. It is also possible muscles can independently influence joint physiology in an adverse way. However, how muscle mechanisms influence osteoarthritis pathology at the knee is unclear when considering studies that have assessed functional activities such as walking, where two apparent outcomes can be discerned. One, that muscles react to the prevailing joint pathology by adopting protective responses, or two, that the responses that are present contribute to the pathology. Moreover, one cannot currently arrive at any universal recommendation for any particular muscular targeted therapy to moderate knee osteoarthritis muscular responses relative to optimizing functional activities. Furthermore, even where muscle appears to have some bearing on osteoarthritic knee joint function, there is no consensus as to whether muscle strength is the key determinant of knee osteoarthritis severity, or whether some other parameter is of greater import.

In light of this conundrum, more standardized research based on a sound theoretical framework is clearly needed to examine the relevance of muscle structure and function and the progression of knee osteoarthritis. As well, research to examine which muscular responses are protective and which are destructive is strongly indicated. To this end more stringent research designs with clear inclusion and exclusion criteria are desirable to tease out possible pathogenic or confounding factors in gait and electromyographic studies such as disease stage^[35,44], the presence of instability^[44], effusion^[45], proprioception abnormalities^[47], excess body weight^[76,77] fatigue^[78], instability^[79], stiffness^[80], inflammatory cytokines^[81],

gamma-loop dysfunction^[82], or related muscle forces at the knee during gait^[83]. Whether rate of force development, muscle endurance and/or muscle power, muscle imbalance, muscle force steadiness or neuromuscular efficiency are more profound functional determinants than strength^[13,31,41,80,84-86] should also be examined. Which interventions produce the best functional outcomes and why should be examined as well to better understand the muscular mechanisms underpinning functional weightbearing activities in patients with varying degrees of knee joint osteoarthritis. Until then, it is recommended that careful individualized neuromuscular assessments be conducted before assuming that muscular variations from the norm exist, and that these require intervention to advance functional activities and prevent excess knee joint damage. Moreover, as observed by Eckstein *et al*^[87] and Rudolfer *et al*^[88] whether universal recommendations to strengthen the knee muscles in all cases of knee joint osteoarthritis is valid should be carefully examined.

CONFLICT OF INTERESTS

No conflict of interest or financial interest was declared.

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