Knee osteoarthritis (OA) is a leading cause of disability among older adults, and the incidence of this pathology is expected to dramatically increase over the next 2 decades. Patients with knee OA demonstrate reduced functional capacity that can be attributed to joint pain, stiffness, and loss of muscular strength of the lower extremity muscles. Although OA is diagnosed and defined as a loss of hyaline cartilage within the joint, muscle impairments associated with the disease may be the primary underlying cause of functional impairments, and muscle dysfunction may actually precede and expedite the cartilage deterioration. As such, knee OA cannot solely be considered a disease of the cartilage, and clinical management of the disease must also take into account associated muscular impairments.

Muscle impairments in subjects with Knee Oa

Quadriceps impairment in subjects with knee OA is well documented in the literature (Table 1). The quadriceps muscle is commonly tested by torque generation capability (peak torque generation) is an important determinant of physical function in subjects with knee OA. In addition to force output, other measures of muscle function are related to physical function, and muscles other than quadriceps are also impaired in patients with knee OA. Therefore, the purpose of this article is fourfold: (1) to describe muscle impairments in subjects with knee OA; (2) to explore the relationship between muscle impairments and physical function; (3) to explain the potential role of muscle impairments in the onset and progression of knee OA; and (4) to summarize the best evidence examining the effectiveness of exercises that target muscle impairments in patients with knee OA.

Results: Quadriceps, hamstrings, and hip muscles are significantly impaired in subjects with knee OA compared with age-matched controls. Muscle strength, especially quadriceps, is a major determinant of both performance-based and self-reported physical function. Whether stronger quadriceps is protective against knee OA onset and progression is not clear. Exercise therapy, including global and targeted resistance training, is effective in reducing pain and improving function in subjects with knee OA.

Conclusions: Subjects with knee OA have significant muscle impairments. These muscle impairments affect physical function and should be targeted in therapy. Further research is needed to explore the relationship between quadriceps strength and knee OA initiation and progression and to determine the optimal exercise prescription that augments outcomes in this patient population.

Keywords: Osteoarthritis, Impairment, Functional limitation, Knee, Exercise
Isometrically, peak quadriceps torque occurs between 45° to 70°. Isometric quadriceps strength deficits in subjects with knee OA range from 10% to 56% (Table 1). Concentric isokinetic tests (Table 1) show that patients with OA demonstrate strength deficits ranging between 11% and 56% compared with healthy controls.11,23

| Reference                  | Osteoarthritis | Control | Test Mode                     | Difference (%)<sup>a</sup> |
|----------------------------|----------------|---------|-------------------------------|----------------------------|
| Pap<sup>46</sup>           | 222 (60)       | 85 (64) | Isometric, 90° knee flexion    | 42                         |
| Palmieri-Smith<sup>45</sup>| 188 (100)      | 160 (100)| Isometric, 90° knee flexion    | 22                         |
| Hortobágyi<sup>23</sup>   | 20 (75)        | 20 (75) | Isometric, 65° knee flexion    | 56                         |
|                            |                |         | Isokinetic concentric, 90°, 180°/s | 56                         |
|                            |                |         | Isokinetic eccentric, 90°, 180°/s | 76                         |
| Gapeyeva<sup>18</sup>     | 10 (100)       | 10 (100)| Isometric, 90° knee flexion    | 48                         |
| Liikavainio<sup>13</sup>  | 54 (0)         | 53 (0)  | Isometric, 70° knee flexion    | 20                         |
| Hurley<sup>26</sup>       | 103 (63)       | 25 (72) | Isometric, 90° knee flexion    | 30                         |
| Cheing<sup>9</sup>        | 66 (86)        | 10 (50) | Isometric, 30° knee flexion    | 10                         |
|                            |                |         | Isokinetic concentric, 60° knee flexion | 27                         |
|                            |                |         | Isokinetic concentric, 90° knee flexion | 25                         |
| Heiden<sup>20</sup>       | 54 (55)        | 27 (67) | Isometric, 90° knee flexion    | 23                         |
| Tar<sup>16</sup>          | 60 (100)       | 30 (100)| Isometric, 30° knee flexion    | 19                         |
|                            |                |         | Isokinetic concentric, 60° knee flexion | 19                         |
|                            |                |         | Isokinetic concentric, 180°/s  | 23                         |
| Diracoglu<sup>11</sup>    | 51 (100)       | 43 (100)| Isokinetic concentric, 60°/s   | 20                         |
|                            |                |         | Isokinetic concentric, 180°/s  | 19                         |
|                            |                |         | Isokinetic concentric, 240°/s  | 11                         |
| Messier<sup>37</sup>      | 15 (73)        | 15 (73) | Isokinetic concentric, 60°/s   | 28                         |
| Thomas<sup>39</sup>       | 22 (100)       | 13 (100)| Isometric, 90° knee flexion    | 11                         |
| Berth<sup>5</sup>         | 50 (64)        | 23 (65) | Isometric, 90° knee flexion    | 37                         |
| Jan<sup>28</sup>          | 55 (100)       | 33 (100)| Isometric, 60° knee flexion    | 32                         |
|                            |                |         | Isokinetic concentric, 30°/s   | 37                         |
|                            |                |         | Isokinetic concentric, 180°/s  | 39                         |
| Fisher<sup>15</sup>       | 90 (50)        | 104 (60)| Isometric, 90° knee flexion    | 54                         |
| Lewek<sup>32</sup>        | 12 (42)        | 12 (50) | Isometric, 90° knee flexion    | 24                         |
| Hall<sup>19</sup>         | 21 (81)        | 21 (81) | Isometric, 60° knee flexion    | 20                         |
| Slemenda<sup>63</sup>     | 112 (56)       | 294 (48)| Isokinetic concentric, 60°/s   | 16                         |
| Rice<sup>47</sup>         | 15 (53)        | 15 (53) | Isometric, 90° knee flexion    | 32                         |
| Emrani<sup>12</sup>       | 20 (NR)        | 20 (NR) | Isokinetic concentric, 90°/s   | 31                         |
|                            |                |         | Isokinetic concentric, 150°/s  | 31                         |

<sup>a</sup>Difference = (mean value of control group – mean value of osteoarthritis group) / mean value of control group.

<sup>b</sup>No radiographic evidence of osteoarthritis and no pain.
The disparity between patients with and without knee OA is even more dramatic during eccentric strength tests, with subjects with knee OA demonstrating 76% eccentric quadriceps strength deficits at 90° per second and 180° per second. Differences in the reported magnitude of strength deficits between these studies can be partly attributed to differences in the subjects’ characteristics, OA severity, and the definition of the control group.

The strength deficits (Table 1) are derived from the involved knee in subjects with unilateral involvement and from the more involved knee in subjects with bilateral symptoms. The contralateral knee in subjects with unilateral or bilateral radiographic OA cannot be considered free of impairments. Compared with healthy controls, even the contralateral leg showed concentric isokinetic quadriceps strength deficits of 16% at 30° per second and an isometric quadriceps strength deficit of 22% to 26% when tested at 90° of knee flexion.5,10 Given these findings, clinicians should use age-matched healthy controls. Interventions that target muscle dysfunction should address impairments in both limbs, not simply the affected or more symptomatic joint.

The 2 main factors that determine the muscle’s force production capability are the muscle cross-sectional area and the ability of the nervous system to fully activate the muscle. Ikeda et al reported 12% reduction in quadriceps cross-sectional area in women with radiographic evidence of knee OA compared to women without radiographic evidence of knee OA, although no differences were observed in the cross-sectional area of the hamstrings.27 In Kellgren/Lawrence grade 4 knee OA, Petterson et al reported a 12% reduction in quadriceps cross-sectional area of the involved leg compared to the contralateral leg. In the same study, quadriceps cross-sectional area explained 27% of quadriceps isometric strength using specimens from vastus medialis muscle in patients undergoing total knee arthroplasty. Fink et al demonstrated atrophy of type 2 muscle fibers, and 52% of the subjects demonstrated atrophy of type 1 muscle fibers. Evidence of reinnervation was seen in 15% of the subjects for type 1 fibers and 37% of the subjects for type 2.

The ability of the nervous system to fully activate the muscle plays a major role in determining the muscle’s force production capacity. Quadriceps volitional activation accounted for 40% of quadriceps strength in patients with knee OA.7 The term arthrogenic muscle inhibition is commonly used for the inability to fully activate the muscle secondary to joint dysfunction.51 To fully activate muscle depends on the ability to recruit all motor units at an optimal firing rate.30 Failure to activate muscle fully indicates inability to recruit all motor units and/or reduction in firing rate. The ability to activate the quadriceps muscle is commonly examined using 2 percutaneous electrical stimulation techniques: burst superimposition and twitch interpolation.46

Pietrosimone et al conducted a meta-analysis of quadriceps volitional activation in subjects with knee OA.24 Fourteen individual studies were included, and a weighted activation mean was calculated for the involved limb, contralateral limb, and limb of control subjects. The weighted average accounted for the number of subjects in each study, thus giving more weight to studies with larger sample size. The weighted activation mean was 82.2% (95% confidence interval [CI], 81.4%-83.3%) for the involved limb, 81.7% (95% CI, 80%-83.3%) for the contralateral limb, and 90% (95% CI, 88.9%-91.7%) for the control limb. Only 5 of the 14 studies had quadriceps activation data for both the involved and contralateral limbs. The involved limb weighted activation mean was 76.8% (95% CI, 74.8%-78.8%). This suggests that patients with knee OA exhibit bilateral quadriceps activation deficits compared to healthy controls, further supporting the notion that the contralateral limb is not free from impairments. Despite the bilateral activation deficit, the meta-analysis also provides evidence that the involved limb exhibits lower quadriceps activation compared to the contralateral limb.

The exact mechanism for quadriceps activation deficits in knee OA is not fully understood. Quadriceps activation deficits are largely due to an alteration in knee joint sensory receptors, which reduces the excitability of the alpha motoneurons via spinal and/or supraspinal mechanisms.26,27 In knee OA, a number of factors could alter the afferent discharge of knee sensory receptors, including degenerative changes to joint structures, joint effusion, inflammation, and joint laxity. Three spinal reflex pathways are possibly involved: group I, nonreciprocal (I b) inhibition, flexion reflex, and gamma loop.26,51

In addition to peak force production, other metrics of muscle function include steadiness, rate of force development, and endurance.5,18,23,65 In a case-control study, submaximal quadriceps force accuracy and steadiness were calculated in subjects with knee OA and healthy controls.53 Quadriceps force error is the difference between the generated force and the target force, while the quadriceps force steadiness is the ability to maintain a steady submaximal force. Subjects with knee OA exhibited 89% more error and 155% less steady force compared to healthy controls. The rate of force development was 60% lower in subjects with knee OA compared to healthy controls.54 Knee OA subjects had 67% lower quadriceps endurance and 60% lower extension angular velocity during knee extension compared to healthy controls.55

Although assessment of quadriceps function remains the gold standard of muscle assessments in knee OA research, subjects with knee OA also have well-documented hamstrings strength deficits (Table 2). Isometric deficits range from 4% to 35%.4 During concentric isokinetic tests, deficits ranged from 7% to 38%.11,12,18,20,33,68 Hip muscle strength in subjects with knee OA (Table 2) showed isometric deficits ranging from 16% in extension to 27% in external rotation. Concentric isokinetic deficits range from 22% in hip abductors to 64% in hip extensors.

References 9, 11, 12, 15, 19, 20, 28, 33, 37, 51, 63, 68.

*References 9, 15, 19, 20, 28, 33, 51, 68.
Table 2. Hamstrings and hip muscles deficit in subjects with knee osteoarthritis compared with healthy controls.

| Reference  | Osteoarthritis | Control | Test Mode                      | Muscle Group | Difference (%) |
|------------|----------------|---------|--------------------------------|--------------|----------------|
| Liikavainio | 54 (0)         | 53 (0)  | Isometric, 70° knee flexion     | Hamstrings    | 13             |
| Cheing      | 66 (86)        | 10 (50) | Isometric, 90° knee flexion     | Hamstrings    | 19             |
| Heiden      | 54 (55)        | 27 (67) | Isometric, 90° knee flexion     | Hamstrings    | 4              |
| Tan         | 60 (100)       | 30 (100)| Isometric, 30° knee flexion     | Hamstrings    | 16             |
|            |                |         | Isometric, 60° knee flexion     | Hamstrings    | 13             |
|            |                |         | Isokinetic concentric, 60°/s    | Hamstrings    | 29             |
| Diracoglu   | 51 (100)       | 43 (100)| Isokinetic concentric, 60°/s    | Hamstrings    | 29             |
|            |                |         | Isokinetic concentric, 180°/s   | Hamstrings    | 15             |
| Messier     | 15 (73)        | 15 (73) | Isokinetic concentric, 60°/s    | Hamstrings    | 29             |
| Jan         | 55 (100)       | 33 (100)| Isometric, 45° knee flexion     | Hamstrings    | 29             |
|            |                |         | Isokinetic concentric, 30°/s    | Hamstrings    | 30             |
|            |                |         | Isokinetic concentric, 180°/s   | Hamstrings    | 38             |
| Fisher      | 90 (50)        | 104 (60)| Isometric, 14° knee flexion     | Hamstrings    | 35             |
|            |                |         | Isometric, 29° knee flexion     | Hamstrings    | 35             |
| Hall        | 21 (81)        | 21 (81) | Isometric, 45° knee flexion     | Hamstrings    | 13             |
| Slemenda    | 112 (56)       | 294 (48)| Isokinetic concentric, 60°/s    | Hamstrings    | 7              |
| Rice        | 15 (53)        | 15 (53) | Isometric, 90° knee flexion     | Hamstrings    | 14             |
| Emrani      | 20 (NR)        | 20 (NR) | Isokinetic concentric, 90°/s    | Hamstrings    | 25             |
|            |                |         | Isokinetic concentric, 150°/s   | Hamstrings    | 30             |
| Sled        | 40 (57)        | 40 (57) | Isokinetic concentric, 60°/s    | Hip abductors | 22             |
| Hinman      | 89 (48)        | 23 (70) | Isometric, sitting, 90° hip and knee flexion | Hip flexors | 26             |
|            |                |         | Isometric, supine, 20° hip flexion and extended knee | Hip extensors | 16             |
|            |                |         | Isometric, supine, 0° hip abduction and extended knee | Hip abductors | 24             |
|            |                |         | Isometric, supine, 0° hip abduction and extended knee | Hip adductors | 26             |
|            |                |         | Isometric, sitting, 90° hip and knee flexion | Hip internal rotators | 20             |
|            |                |         | Isometric, sitting, 90° hip and knee flexion | Hip external rotators | 27             |
| Costa      | 50 (88)        | 50 (88) | Isokinetic concentric, supine, 30°, 60°, 180°/s | Hip flexor | 40³             |

(continued)
Patients with knee OA self-reported outcome measures do not correlate highly with performance-based outcome measures, suggesting that these metrics do not provide comparable information. Patients with knee OA tend to overestimate function; questionnaires tend to be driven by the subject’s pain level. Quadriceps strength is related to functional tasks, such as standing up from a chair, going up and down stairs, and level surface walking. In a cross-sectional study, quadriceps peak force generation explains about 40% of the variance in stair climbing performance. Quadriceps strength is a significant predictor of getting down to and up off the floor, and predicted performance in the 6-minute walk test and the “timed up and go” test using a regression analysis. Quadriceps activation deficits moderate the relationship between quadriceps strength and physical function. Quadriceps peak torque generation is also related to self-reported physical function (Western Ontario and McMaster Universities Osteoarthritis Index [WOMAC] questionnaire). Quadriceps force error and quadriceps force unsteadiness are related to the 18-m walking task, “get up and go” test, and stair ascent and descent. Quadriceps endurance and maximal angular velocity during knee extension are related to the time required to walk 15 m. Lower quadriceps endurance and less angular velocity during knee extension was related to the need for more time to complete the 15-m walk.

Hamstrings concentric isokinetic strength (peak torque) is a significant predictor of the performance of a stair climbing task. Hamstrings isometric strength significantly correlates with stair climbing, standing from sitting, walking, and lifting an object from the floor. In a case-control study, hamstrings strength negatively correlates with the composite score and the physical function subscale of the WOMAC questionnaire, indicating that patients with weaker hamstrings have higher self-perceived functional limitations.

**MEASURES OF MUSCLE FUNCTION AND PHYSICAL FUNCTION**

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**MUSCLE IMPAIRMENTS AND KNEE OA INITIATION AND PROGRESSION**

Lower extremity muscles provide functional stability to the knee joint and act as a shock absorber. Quadriceps strength is related to the rate of lower extremity loading in healthy women; subjects with weaker quadriceps have higher loading rates. Higher loading rates may initiate knee OA or cause progression of existing disease. On the contrary, quadriceps strength shows a bivariate relationship with rate of loading, but this relationship was lost after controlling for potential confounders including gait speed.

The question is, does knee OA cause quadriceps weakness, or does quadriceps weakness precede the disease onset and contribute to the initiation and progression of the disease? The development of incident radiographic knee OA was monitored over a mean period of 31 months in 280 subjects with no radiographic evidence of OA in 1 knee. Women who develop incident knee OA had weaker quadriceps relative to body weight. A prospective cohort study examined the relationship among baseline quadriceps strength, hamstrings:quadriceps ratio, and the development of incident radiographic or symptomatic knee OA at 30 months. Quadriceps strength was a significant predictor of incident symptomatic knee OA but not incident radiographic knee OA. The relationship between quadriceps strength and proprioception and the initiation of radiographic knee OA is not clear.
and symptomatic knee OA was also examined. Regardless of the joint position sense, those with stronger quadriceps had a reduced risk of development of symptomatic knee OA. Quadriceps strength and joint position sense were not predictive of incident radiographic knee OA. Baseline quadriceps strength is not related to knee OA progression, but with knee malalignment, stronger quadriceps was associated with knee OA progression. Similarly, with knee laxity, stronger quadriceps was associated with knee OA progression.

In a prospective cohort magnetic resonance imaging study, stronger quadriceps reduced the likelihood of cartilage loss in the lateral patellofemoral joint (odds ratio, 0.4; 95% CI, 0.2-0.9) but not the tibiofemoral joint (medial compartment: odds ratio, 1; 95% CI, 0.5-1.8; lateral compartment: odds ratio, 1.1; 95% CI, 0.5-2.5). Stronger quadriceps strength had a chondroprotective effect; knee malalignment did not increase cartilage loss with strong quadriceps. In a recent prospective cohort study, weaker quadriceps at baseline was associated with an increase in joint space narrowing (odds ratio, 1.66; 95% CI, 1.26-2.19) at a 30-month follow-up in women only. The hamstrings:quadriceps ratio did not influence joint space narrowing in either men or women.

Few randomized clinical trials have included quadriceps strengthening exercises and radiographs to determine knee OA initiation and progression. Mikesky et al randomly assigned subjects with and without radiographic knee OA to a quadriceps and hamstring training program or a range of motion program. Thirty months later, both groups showed decline in quadriceps and hamstrings strength. There was no difference in medial joint space narrowing between the strength training and the range of motion group. Messier et al randomly assigned subjects with knee OA into a diet group, exercise group, diet and exercise group, or a control group. Medial and lateral joint space width was not different among the groups over 18 months.

**TARGETING MUSCLE IMPAIRMENTS: THE EVIDENCE**

Reducing knee pain, improving physical function, and reducing physical disability are the primary goals of OA interventions. Exercises are considered an integral part of knee OA management, and international guidelines recommend exercises. A Cochrane systematic review examined the effectiveness of land-based therapeutic exercises in reducing pain and improving self-reported physical function in subjects with knee OA. Thirty-two randomized and quasi-randomized controlled trials showed a significant effect in reducing pain with a standardized mean difference of 0.40 (95% CI, 0.30-0.50) and improving self-reported physical function with a standardized mean difference of 0.37 (95% CI, 0.25-0.49). The number needed to treat to benefit was 7 for the WOMAC pain, 6 for the visual analog scale pain, and 8 for the WOMAC physical function (Table 3).

A systematic review examined the effectiveness of resistance training on knee pain, self-reported physical function, physical

| Type of exercise                              | Standardized Mean Difference |
|-----------------------------------------------|------------------------------|
| Simple quadriceps strengthening              | 0.29                         |
| Lower limb muscle strengthening              | 0.53                         |
| Strengthening with aerobic component         | 0.40                         |

| Exercise delivery mode                        | Standardized Mean Difference |
|-----------------------------------------------|------------------------------|
| Individual treatment                          | 0.55                         |
| Class-based program                           | 0.37                         |
| Home program                                  | 0.28                         |

| Number of supervised sessions                 | Standardized Mean Difference |
|-----------------------------------------------|------------------------------|
| 12 or more                                    | 0.46                         |
| Less than 12                                   | 0.28                         |

Table 3. Standardized mean difference of land-based exercises on pain and physical function.
performance, and psychological outcomes in 2832 patients with knee OA.34 Sixteen of the 18 randomized controlled trials included supervised exercise programs, while 2 were home based. Resistance training included isometric,8 isotonic,6,13 isokinetic,36,55 and some functional strength training.2,41 Three training sessions per week were commonly prescribed. A 17.4% mean improvement in muscle strength was seen (effect size, 0.38). Fifty-six percent of the studies reported significant reduction in knee pain following resistance training with large effect size (2.11). In 79% of the studies, physical function significantly improved with a small effect size (0.31). The effect of resistance training on health-related quality of life is inconsistent.

Another systematic review of 10 randomized controlled trials and 2004 participants examined the effectiveness of home-based quadriceps strengthening and aerobic walking on knee pain and self-reported physical function in knee OA patients.53 Quadriceps strengthening was effective in reducing knee pain and improving physical function with pooled effect size of 0.32 (95% CI, 0.23-0.42), and 0.32 (95% CI, 0.23-0.41), respectively. Clinical trials of hip abductor and adductor strengthening reported no change in knee joint loads.5,12,50 The experimental group showed a significant reduction in knee pain, improvement in self-reported and performance-based physical function, as well as a 13% and 19% improvement in hip abductor and adductor strength, respectively.3

**SUMMARY**

The quadriceps femoris muscle is significantly impaired in subjects with knee OA compared to age-matched healthy controls.5,11 Both activation deficit and atrophy contribute to quadriceps weakness.2,48 Muscle impairments in patients with OA are not limited to quadriceps but also involve hamstrings and the muscles of the hip.10,12 Muscle strength, especially quadriceps, is a major determinant of both performance-based and self-reported physical function in subjects with knee OA.3,35 The relationship between quadriceps strength and knee OA initiation and progression is not clear. The evidence supports the benefit of exercise therapy, including global and targeted resistance training, in reducing pain and improving function in subjects with knee OA. OA is a chronic disease, so patients should be encouraged to integrate exercises into their weekly routine and should be educated to the fact that the beneficial long-term effect of exercise is highly dependent on their adherence to their exercise program. The recommendations for exercise therapy in patients with hip and knee OA have been established by a multidisciplinary panel of experts (Table 4).54

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**Table 4. Exercise recommendations.**

| Recommendation |
|----------------|
| Both strengthening and aerobic exercise can reduce pain and improve function and health status in patients with knee and hip osteoarthritis (OA). |
| There are few contraindications to the prescription of strengthening or aerobic exercise in patients with hip or knee OA. |
| Prescription of both general (aerobic fitness training) and local (strengthening) exercises is an essential, core aspect of management for every patient with hip or knee OA. |
| Exercise therapy for OA of the hip or knee should be individualized and patient centered, taking into account factors such as age, comorbidity, and overall mobility. |
| To be effective, exercise programs should include advice and education to promote a positive lifestyle change with an increase in physical activity. |
| Group exercise and home exercise are equally effective, and patient preference should be considered. |
| Adherence is the principal predictor of long-term outcome from exercise in patients with knee or hip OA. |
| Strategies to improve and maintain adherence should be adopted—for example, long-term monitoring/review and inclusion of spouse/family in exercise. |
| The effectiveness of exercise is independent of the presence or severity of radiographic findings. |
| Improvements in muscle strength and proprioception gained from exercise programs may reduce the progression of knee and hip OA. |
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