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Therapeutic exercise for knee osteoarthritis: considering factors that may influence outcome

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While exercise has been shown to be beneficial for reducing pain and improving physical function in individuals with knee osteoarthritis (OA), there are still individuals who do not always respond well to this treatment approach. There are a number of factors that have been shown to influence either the degree of disability and/or the progression of disease in individuals with knee OA. These factors include quadriceps inhibition or activation failure, obesity, passive knee laxity, knee alignment, fear of physical activity and self efficacy. It may be possible that varying levels of these factors might also interfere with an individual's ability to participate in an exercise or physical activity program or minimize the benefits that can be achieved by such programs. This paper examines the influence of these factors on physical function and their potential for altering the outcome of exercise therapy programs for individuals with knee OA. Implications and suggestions for potential adjunctive interventions to address these factors in future research and clinical practice are also discussed.

Key words: **Knee - Osteoarthritis - Exercise, Physical therapy - Rehabilitation.**

In recent years, there have been numerous studies that have demonstrated the effectiveness of exercise and physical activity for individuals with knee osteoarthritis (OA).[1-9] Although exercise and physical activity programs have been found to be beneficial, the overall effects of these interventions have been found to yield small to moderate effects at best for individuals with knee OA.[10, 11] For example, a systematic review of the effectiveness of exercise for reducing pain and improving disability conducted by van Baar *et al.*,[10] yielded moderate effect sizes for reducing pain (effect size range = 0.31 to 0.58) and small effect sizes for improving disability (effect size range = 0.26 to 0.41). Similarly, a more recent systematic review by Fransen *et al.*,[11] demonstrated small to moderate effects for reducing pain (standardized mean difference = 0.39) and physical function (standardized mean difference = 0.31). These findings suggest that there is clearly room for improvement in designing and implementing exercise and physical activity programs to maximize the benefit of these treatments for individuals with knee OA.

There are a number of factors that have been shown to influence either the degree of disability and/or the progression of disease in individuals with knee OA. These factors include quadriceps inhibition or activation failure, obesity, passive knee laxity, knee alignment, fear of physical activity and self efficacy.[12-22] It may be possible that varying levels of these factors might also interfere with an individual's ability to participate in an exercise or physical activity program or minimize the benefits that can be achieved by such programs. Perhaps the overall beneficial effects of exercise and physical activity programs for individuals with knee OA could be improved if we were able to identify and address these factors in a manner that

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would allow some individuals to become more responsive to their rehabilitation programs. The purposes of this paper are to explore potential factors that may influence the outcome of exercise and rehabilitation programs for individuals with knee OA and to make suggestions for addressing these factors in future research and clinical practice.

Quadriceps activation failure

Quadriceps activation failure is the inability to fully activate the quadriceps during maximum effort muscle contraction.[13] This condition has also been referred to as arthrogenous muscle inhibition.[23] Quadriceps activation failure is detected by comparing the maximum isometric quadriceps torque output during voluntary contraction of the muscle with the torque output produced when a supramaximal electrical stimulus is superimposed on a maximum voluntary isometric quadriceps contraction.[12, 13] Activation failure is considered to be present if there is additional torque produced by the muscle when the electrical stimulus is applied, compared to the maximum voluntary isometric torque output without application of the electrical stimulus. The theory is that the electrical stimulus has recruited additional muscle fibers that were not activated prior to application of the stimulus, resulting in the additive torque output effect.

The cause of quadriceps activation failure in patients with knee OA is not fully understood. Although investigators have associated the activation failure with the presence of joint effusion in patients with knee injuries,[24, 27] some patients with knee OA demonstrate quadriceps activation failure in the absence of significant joint effusion.[12] Pain can also result in reduced muscle activation, however, others have reported no correlation between pain and quadriceps activation failure in individuals with knee OA.[12, 13] Hurley, *et al.*, suggested that degenerative changes to joint structures in knee OA may result in altered sensory information from joint mechanoreceptors that, in turn, may reduce the ability to activate the quadriceps femoris muscles.[12]

Individuals with knee OA have been found to exhibit greater quadriceps activation failure compared to age and gender matched control subjects.[12, 23, 28] The presence of quadriceps activation failure has been associated with greater impairment in quadriceps strength and poorer scores on physical performance and self-report measures of physical function in individuals with knee OA.[12, 13] Fitzgerald, *et al.*,[13] recently determined that the presence of quadriceps activation failure can moderate the relationship between strength and function in individuals with knee OA. Specifically, they found that subjects with knee OA who demonstrate quadriceps activation failure were more affected by quadriceps weakness than those who were weak but did not demonstrate quadriceps activation failure, with regard to measures of physical function.

It may be possible that larger amounts of quadriceps activation failure combined with greater weakness may limit the degree to which voluntary exercise can restore quadriceps strength and improve physical function in patients with knee OA. In individuals with traumatic knee injuries, a higher degree of quadriceps activation failure prior to rehabilitation was found to limit the recovery of quadriceps strength, even after an intensive lower extremity strengthening program.[29] It is believed that, in the presence of activation failure, the quadriceps muscles may not be able to produce enough muscle tension during volitional exercise to render a beneficial effect from training.[29] In individuals with knee OA, there may be a subgroup of patients with weak quadriceps muscles combined with higher degrees of activation failure that may not be able to respond favorably to volitional exercise therapy programs for this reason. This could explain, in part, the overall modest effects of exercise therapy in restoring quadriceps strength, reducing pain, and improving function in patients with knee OA. Individuals who exhibit relatively large magnitudes of quadriceps activation failure may need specialized treatment interventions designed to improve muscle activation to supplement volitional exercise programs in order to achieve maximum benefit from rehabilitation.

What is not yet clear is how much quadriceps activation failure is required to interfere with the beneficial effects of voluntary strengthening exercises. One study measured changes in quadriceps activation failure, quadriceps strength, and physical function in response to a volitional exercise program in individuals with knee OA.[5] The results of this study appeared to be some improvements in quadriceps activation, improvement in quadriceps strength, and improvement in physical function for the exercise groups overall, however, there was no attempt in these studies to determine whether the pre-rehabilitation magnitude of quadriceps activation failure could predict the degree of improvement in these measures following rehabilitation.[5] Establishing the value of quadriceps activation failure that would affect the outcome of exercise therapy may be important in refining rehabilitation programs for individuals with knee OA. Specifically, rehabilitation programs could be tailored to meet the specific needs of the individual patient based on the presence or absence of a clinically meaningful level of pre-treatment quadriceps activation failure when patients have significant quadriceps weakness. Those who are weak but exhibit lower values of activation failure may only require standard exercise therapy. Those who are weak with larger values of activation failure may require adjunctive treatments such as neuromuscular electrical stimulation and/or electromyographic biofeedback training in addition to standard exercise therapy, to address the quadriceps activation failure problem. We are currently conducting a clinical trial to determine if pretraining activation failure values can predict the outcome of exercise therapy for quadriceps strengthening.

Obesity

Studies have shown that obesity is a risk factor in the development and progression of knee OA.[18, 19] In contrast, weight loss may reduce the risk of developing symptomatic knee OA.[30] Obese individuals with knee OA tend to have greater levels of disability compared to those with knee OA who are not obese.[31] In a 3 year longitudinal study of 257 subjects with knee OA, Sharma, *et al.*,[32] reported that greater body mass index (kg/m^2) at baseline increased the risk of either having lower physical function scores or actually regressing in physical function scores over the 3 year period.

Jadelis, *et al.*,[33] reported that scores on balance testing were adversely affected by obesity, regardless of the level of lower extremity strength in individuals with knee OA. This finding might suggest that improving strength alone in individuals who are obese may not be enough to adequately address factors that might relate to reduced physical function. Recently, Messier, *et al.*,[20] conducted a relatively large randomized trial examining the combination of diet and exercise on physical function in 252 elderly individuals (60 years or older) with knee OA who were also considered obese (body mass index ≥ 28 kg/m^2). Subjects were randomized to either a group that received a regimented diet program only, an exercise program only, a combination of the diet and exercise programs, or a control group that received a healthy lifestyle education program. Following an 18 month intervention period that combined both facility-based and home-based applications of the treatments, the group that received both diet and exercise exhibited the greatest improvements in the Western Ontario and McMaster's University Osteoarthritis Index (WOMAC) function and pain scores, weight reduction, and performance on the 6 minute walk for distance test and stair climb for time test.[20] This study clearly supports the idea that subjects who are obese with knee OA need to supplement their exercise program with a dietary intervention that is designed to reduce weight, in order to achieve the greatest benefit for improving physical function.

Knee alignment

Alterations in joint alignment can affect the area of load distribution across joint surfaces. It has been estimated that a 4° to 6° increase in varus alignment of the knee can increase the loading of the medial knee compartment from 70% to 90% during single limb weight bearing.[17] Sharma, *et al.*,[34] reported that the amount of varus and valgus alignment of the knee was significantly correlated with increases in the progression of compartmental knee OA. The presence of excessive varus alignment resulted in a 4 fold increase in the odds of medial compartment OA progression, and excessive valgus alignment resulted in a 5 fold increase in odds of lateral compartment OA progression.[34] Furthermore, subjects with knee OA who had varus and valgus alignments in both knees of greater than 5° demonstrated greater functional deterioration over an 18 month period compared to those whose varus and valgus alignments were less than 5°.[34]

The relationship between quadriceps strength and progression of knee OA may also be altered by varus/valgus alignment. Sharma *et al.*,[16] reported that subjects with greater quadriceps strength who also exhibited greater degress of varus/valgus malalignments were more likely to have radiographic progression of knee OA over an 18 month period than those who had less quadriceps strength and similar degrees of malalignment. Sharma *et al.*,[16] suggested that varus/valgus malalignment could alter the outcome of quadriceps strengthening programs for individuals with knee OA. The responsiveness to a strengthening program, however, was not observed in Sharma et al's study. Further study is needed to determine if the degree of varus/valgus malalignment can negatively affect the outcome of rehabilitation programs. It may be that interventions that target the malalignments might be needed as an adjunct to exercise programs to improve the overall beneficial effects of rehabilitation for those individuals who have significant varus/valgus malalignments.

Joint malalignments at the knee can be addressed to some degree through the use of orthotic devices and shoe inserts. Orthotic devices are commercially available that can unload the medial compartment of the knee by applying a valgus load to the knee through specially designed axes and straps.[35-37] These braces have been shown to reduce pain and improve function in individuals with medial compartment knee OA.[35-37] Pollo, *et al.*,[37] also demonstrated that calculated varus torques were reduced by 13% and medial compartment compression loads were reduced by 11% with the unloader brace. In the present author's clinical experience, some patients are not compliant with wearing this type of brace due to complaints of heaviness and bulkiness. Clinicians should consider issues of compliance with these orthotic devices. In this author's experience, patients who wear the brace for specific activities seem to be happier with these orthotic devices than those who attempt to wear them for all -purpose use.

The use of a lateral wedge shoe insert for individuals with medial compartment knee OA has also been found to be useful in reducing pain and improving function.[38, 39] Kerrigan, *et al.*,[40] reported that a 5° wedge could reduce the varus moment at the knee in 15 subjects with medial compartment knee OA. The theory is that the lateral wedge may encourage more valgus loading on the knee, countering the varus moment. It should be noted that lateral wedge shoe inserts seemed to be more effective for individuals with minimal to moderate degrees of OA and that individuals with more severe OA or malalignments may not always respond favorably to this intervention.[38]

Toda has developed a lateral wedge combined with a sub-talar strap for treating individuals with medial compartment knee OA.[41, 42] Toda reported that the subtalar strap stabilizes the subtalar joint enough to allow the wedge to affect the femorotibial angle. Toda reported an average of 3.1° reduction in the varus angle at the knee when the wedge was combined with the sub-talar strapping, compared to use of the wedge without sub-talar strapping.[41] Following 8 weeks of the intervention, subjects receiving the wedge with the sub-talar strapping reported significant improvements in pain and walking distance.[41] These subjects, however, reported having difficulty ambulating with the device on uneven surfaces.

Knee Instability

Recently, we have reported that a significant number of individuals with knee OA complain of knee instability that is severe enough to affect their ability to perform activities of daily living.[43] In our study, we defined the complaint of knee instability as a sensation of buckling, shifting, or giving way at the knee during functional activities. We found that this report of knee instability was associated with poorer functional performance, even after controlling for other factors that could affect function in individuals with knee OA, such as pain, muscle weakness, and reduced joint mobility.[43] We concluded that knee instability is a prevalent problem in individuals with knee OA that contributes to disability above and beyond what can be expected from the presence of other impairments.

Knee instability experienced by individuals with knee OA is most likely a multi-factorial problem, which may be the result of factors such as increased capsulo-ligamentous laxity, structural damage to the knee, and altered lower extremity muscular strength and neuromuscular control. Investigators have reported increased passive knee laxity in individuals with knee OA.[14, 44] Passive varus/valgus laxity appears to be more prevalent in knee OA than anterior-posterior laxity.[14] The laxity has been described as a "pseudo-laxity" because although capsuloligamentous structures remain intact, it is believed that the laxity results from reduced tension in the joint capsule and ligaments, secondary to progressive degenerative changes in joint and increased joint space narrowing.[14] In short, the passive restraints slacken as the disease process progresses. Sharma, *et al.*, reported that greater amounts of passive varus/valgus laxity were associated with greater amounts of bony attrition and joint space narrowing of the knee, providing some support for the notion of pseudo-laxity.[14]

Varus/valgus laxity at the knee can influence physical function in individuals with knee OA. Recently, Sharma, *et al.*,[32] reported that increased varus/valgus laxity at baseline increased the odds of either poor or diminished self-reported function scores over a 3 year period in 257 individuals with knee OA. This finding remained stable even after controlling for age, body mass index, knee pain, and radiographic severity of knee OA. In an earlier study, Sharma, *et al.*,[45] demonstrated that, in the presence of increased knee laxity, the relationship between quadriceps strength and physical function was diminished. This finding might suggest that for individuals with excessive varus/valgus knee laxity, simply strengthening the quadriceps may not be enough to improve physical function and that adjunctive interventions designed to address the knee laxity might also be needed to improve the maximum benefit of therapeutic exercise.

Knee instability and laxity in individuals with knee OA may contribute to altered movement patterns that in turn could contribute to reduced functional ability and progression of disease. Lewek, *et al.*,[15] investigated the effects of frontal plane laxity on gait variables in individuals with medial compartment knee OA (N = 12) compared to age and gender matched controls (N = 12). There was no difference in lateral laxity between groups but there was significantly greater medial laxity in the knee OA group.[15] The knee OA group exhibited less knee flexion excursion, greater knee adduction moments, and greater magnitudes of co-contraction on the medial musculature compared to the control group.[15] Medial laxity accounted for approximately 21% of the variability in co-contraction and adduction moment values.[15] Seven of 12 subjects in the knee OA group reported having symptoms of knee instability and the knee OA group had significantly worse scores on a self-reported measure of function compared to control subjects.[15] These alterations in gait variables represent a stiffening of the knee in individuals with knee OA that may be an attempt to control knee instability. We have also found that individuals with knee OA walk and step down from a curb with less knee motion and with greater amounts of co-contraction in the muscles about the knee compared to age and gender matched control subjects.[46] Although this stiffening pattern might help to reduce the instability, it may reduce the ability to perform more complex motor tasks needed for higher level functioning and it may also contribute to greater compression and excessive loading across the joint. For these individuals, rehabilitation programs may have to be developed that include activities that improve knee instability but discourage the stiffening pattern of the lower extremity.

Because individuals with knee OA report symptoms of knee instability that are similar to those of individuals with knee ligament injury, and that the findings by Lewek, *et al.*,[15] and Childs, *et al.*,[46] seem to indicate they also stiffen the lower extremity similar to individuals who have ligament deficient knees, we hypothesized that intervention approaches that have been found to be beneficial for individuals with ligament injuries might be used as a template in rehabilitation programs for individuals with knee OA. We recently published a case report that described the development and use of perturbation (roller board and tilt board perturbations) and agility training techniques (quick stops and starts, quick changes in direction, lateral and rotational movements, etc.) to be used in conjunction with strengthening and flexibility exercises in a patient with knee OA who had significant complaints of knee instability. Our rationale was that if individuals were to learn how to control the knee in the presence of potentially destabilizing forces that might be encountered during daily life, then these same potentially destabilizing loads should be applied during rehabilitation.[47] This training program was a modification of a similar program we found to be effective in rehabilitating young, athletic, individuals with ACL deficient knees to return to high level physical activity.[48] Following 6 weeks of training, our patient no longer complained of episodes of knee instability and she was able to resume activities such as golf and tennis. We are currently conducting a randomized clinical trial to determine the effectiveness of adding the perturbation and agility training techniques to standard therapeutic exercises for individuals with knee OA.

Impairments at other lower extremity Joints

Overall functional improvement in rehabilitation may be altered if there are persistent impairments existing at other lower extremity joints in addition to the knee. For example, Jadelis, *et al.*,[33] reported that the best dynamic balance scores in their subjects with knee OA were obtained when both the knee and ankle muscles were found to be strong. Even in the presence of weaker knee muscles, if the ankle muscles were strong, dynamic balance scores were relatively good.[33] However, if the ankle musculature was weak, then subjects were less likely to compensate during balance testing for weak knee muscles. Jadelis, *et al.*,[33] stated that their findings illustrate the importance of addressing strength in muscle groups at other joints of the lower extremity in addition to the knee musculature for optimizing the responsiveness to exercise programs in individuals with knee OA.

Cliborne *et al.*,[49] reported that a significant proportion of individuals (45% to 90%, depending on the test used) in their sample of 22 subjects with knee OA exhibited either pain or reduced mobility at the hip in a battery of 4 hip function tests. Subjects who complained of either pain or had reduced motion on at least 1 test underwent a treatment program of manual hip joint mobilization techniques. Immediately following the mobilization treatment, pain and range of motion was significantly improved on repeat testing. It can't be determined from this study whether these responses to the manual therapy treatment resulted in improved overall physical function as there were no measures of general physical function performed in this study. The authors stated that their results indicate that individuals with knee OA are likely to have impairments at other lower extremity joints and identifying and addressing these other impairments may improve the overall effect of rehabilitation.[49]

Perhaps the best treatment effects reported from a therapeutic exercise program for individuals with knee OA in recent years was by Deyle, *et al.*[8] Deyle, *et al.*,[8] compared a group of subjects who received manual therapy combined with a general lower extremity flexibility and strengthening program to subjects who received a subtherapeutic application of ultrasound (placebo group) in improving WOMAC scores and the 6 minute walk test. Subjects in the manual therapy group received joint mobilization techniques to the lumbo-pelvic region, hip, knee, and/or ankle, depending on whether they exhibited pain or reduced mobility at any of these joints on joint mobility testing. Deyle reported 60% improvements in pain and 54% improvements in stiffness and function scales of the WOMAC in the group receiving manual therapy plus exercise.[8] No significant changes were reported in the control group following the intervention period. Differential effects of the manual therapy *versus* the general exercise program could not be determined from this study. However, the study seems to suggest that a comprehensive program that addresses impairments existing in the trunk, hip, and ankles, as well as the knee may be likely to improve the responsiveness of individuals with knee OA to therapeutic exercise programs.

Self efficacy and fear of physical activity

Self efficacy (belief that the individual has the ability to engage in physical activity) and pain related fear of physical activity are factors that can be barriers to a physically active lifestyle and influence the level of disability and progression of disability in individuals with knee OA and knee pain.[21, 22, 32, 50-52] Rejeski, *et al.*,[22] reported that older individuals with chronic knee pain who had a combination of low self efficacy and significant muscular weakness were more likely to exhibit functional decline over a 30 month period compared to other subjects with higher levels of self efficacy who were either strong or weak. Sharma, *et al.*, also reported that higher self efficacy at baseline was associated with maintaining higher levels of function and low baseline self efficacy was associated with remaining at lower levels of function over a 3 year period.[32] Taken together, the data seems to suggest that promoting self efficacy during the course of rehabilitation might help to improve overall physical function even if it is difficult to improve some of the physical impairments associated with knee OA. For example, perhaps the overall effectiveness of a rehabilitation program in improving physical function might be elevated if during the course of treatment the patient obtained a higher degree of self efficacy, even though only modest improvements in impairments such as muscular strength, pain, and joint mobility were achieved.

Heuts, *et al.*,[21] reported that the level of pain-related fear of activity was negatively correlated with WOMAC function scores. Heuts, *et al.*, described an "activity-avoidance focus" (belief that participation in physical activity may cause injury or increase pain) and a "somatic focus" (belief of an underlying somatic-medical condition) of pain-related fear of physical activity behavior. Both of these focuses were negatively associated with the level of physical function in OA subjects. Heuts, *et al.*,[21] hypothesized that individuals with higher levels of pain-related fear of physical activity may be less likely to engage in a physically active lifestyle and would therefore be more prone to a decline in function.

It may be possible to promote self efficacy and reduce fear of physical activity within the exercise therapy setting. There is some evidence that providing a positive environment, where the clinician provides specific feedback and rewards participant effort, can enhance the level of self efficacy beliefs compared to a neutral environment where only vague feedback is given and accomplishments are not rewarded.[53] Simply positively engaging with our patients during the exercise therapy sessions might promote greater levels of self efficacy. Another consideration may be the types of physical activities that are used during the exercise therapy sessions. The agility and perturbation training program we described above exposes the individual to a variety of movement problems and provides a potential mechanism for solving these problems. It gives the individual an opportunity to practice challenging movement tasks in a supervised manner that may increase the individual's confidence that he or she can safely engage in a variety of physical activities and reduce fear of physical activity. Supplementing exercise programs with other types of functional retraining techniques that might include the practice of stair climbing, basic and advance transfers, and other challenging activities of daily living might also serve to improve self efficacy and reduce fear of physical activity.

Radiographic severity of knee osteoarthritis

Although investigators have reported either weak or no associations between the radiographic severity of knee OA and pain or functional ability,[43, 54-57] baseline radiographic severity may play a role in predicting responsiveness to rehabilitation.[9] Fransen, *et al.*,[9] reported that the degree of joint space narrowing on radiographic examination at baseline modified responsiveness to exercise therapy. Subjects with greater narrowing of the joint space did not respond as well to exercise as those who had less severe changes.[9] Similarly, Sasaki, *et al.*,[38] noted that lateral wedge shoe inserts seemed to be more effective for individuals with minimal to moderate degrees of knee OA and that individuals with more severe knee OA may not always respond favorably to this intervention. Fransen, *et al.*,[9] stated that perhaps physical therapy should be initiated in the early stages of the disease to achieve maximum benefits, and that early screening and preventative exercise therapy programs may be a more cost-effective approach to management of knee OA over the long-term. Another consideration is that perhaps prolonged attempts at rehabilitation are pointless in those patients that have severe radiographic changes combined with significant degrees of pain and disability. While some patients with severe radiographic knee OA might receive benefits from rehabilitation, when these patients don't respond to rehabilitation, more aggressive medical-surgical interventions are warranted.

Conclusions

In this paper a number of factors have been identified that may have the potential to influence the outcome of exercise therapy and rehabilitation for individuals with knee OA. The effect knee OA has on pain and function for a given individual appears to be related to a variety of individual characteristics. Although the literature clearly supports the beneficial effects of exercise for individuals with knee OA, the relatively modest effects may be explained by the inability of the exercises to address some of these other factors that might place barriers on the ability of patients to achieve maximum benefits from the exercise programs. More research is needed to determine how these factors may influence the outcome of exercise therapy programs. When we have a better understanding of the factors that influence the outcome of exercise therapy for knee OA, we can then develop strategies to address these factors and improve the overall effectiveness of rehabilitation for individuals with knee OA.

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