

## Original Article

# Ischemic Preconditioning Improves Hip Abductor Strength and Power in Patients with Symptomatic Knee Osteoarthritis

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## Abstract

**Objective:** To investigate the effect of ischemic preconditioning (IC) on bilateral hip abductor strength, fatigue, and power in patients with knee osteoarthritis (KOA). **Methods:** Participants (n=10) with KOA completed isokinetic and isometric hip abductor assessments on a Biodex dynamometer both before and after IC. IC was administered during a single session and consisted of 5 minutes of inflation (225mmHg) followed by 5 minutes of reperfusion for 50 minutes. Changes in strength and endurance measures before and after IC were compared using paired t-tests and magnitude of significant differences were reported using Cohen's *d* effect sizes. **Results:** Isokinetic hip abductor peak torque ( $d=.42$ ,  $p=.027$ ) and average power ( $d=.57$ ,  $p=.029$ ) in the involved limb, and isokinetic peak torque ( $d=.37$ ,  $p=.044$ ) in the uninvolved limb increased significantly after IC compared to baseline. There were no changes in isokinetic average power in the uninvolved limb, or isometric peak torque and fatigue index in both limbs after IC ( $p=.13-.77$ ). **Conclusions:** A single session of IC improved hip abductor strength in both limbs and power in the involved limb in KOA patients. IC should continue to be investigated as a safe and clinically convenient intervention that can supplement traditional modalities to improve muscle function in KOA.

**Keywords:** Blood Flow Restriction, Function, Knee Pain, Muscle

## Introduction

Knee osteoarthritis (KOA) is one of the most common joint disorders in the world and has a prevalence of about 14-45%<sup>1-3</sup>. KOA causes morphological changes and presents with pain as a primary symptom that affects activities of daily living and quality of life<sup>4</sup>. Exercise therapy, especially through prescribed walking, is one of the most cost-effective treatment options for KOA<sup>5-8</sup>. However, changes in gait mechanics and compensatory behaviors including increased

trunk lean in individuals with KOA<sup>9</sup> may, directly or indirectly, impair their ability to engage in exercise. In fact, research has demonstrated that greater fatigability, which may be linked to energetically costly gait compensations like trunk lean, as well as certain gait alterations are associated with lower levels of physical activity in people with KOA<sup>10,11</sup>.

Changes in gait mechanics, and in turn, decreases in physical activity, may also be related to decreased muscle strength. In addition to decreased knee flexor and extensor strength, which is linked to reduced physical activity<sup>12</sup>, individuals with KOA have hip abductor weakness<sup>13,14</sup>. Hip abductor weakness is associated with KOA disease severity and progression<sup>15</sup>, presumably through its effect on medial compartment knee joint loading. Therefore, hip abductor strengthening and walking is often prescribed as a treatment option in KOA aiming to improve pelvic control, functional outcomes, and pain<sup>16,17</sup>.

Although improved hip abductor strength in those with KOA improves function and pain<sup>18,19</sup>, exercise interventions have a high dropout rate due to common barriers, such as

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time and economic constraints<sup>20,21</sup>. Home exercise programs, although lacking the constraints of other exercise programs, still need to address compliance issues in this population<sup>6,21</sup>. There is a need for more effective and clinically convenient interventions that improve functional outcomes with minimal pain. Ischemic preconditioning (IC), which exposes the limb to brief periods of ischemia followed by reperfusion in repeated cycles<sup>22,23</sup>, has the potential to improve outcomes alone or in conjunction with other interventions. In stroke patients, IC has been shown to improve muscle hypertrophy and strength with both local and systemic benefits<sup>24,25</sup>. IC may therefore also benefit people with KOA who exhibit significant strength deficits. Thus, the purpose of this study was to investigate the effect of a single session of IC on bilateral hip abductor strength and endurance in participants with symptomatic KOA. We hypothesized that hip abductor strength, endurance, and power would increase after a single session of IC in both the involved and uninvolved limbs.

## Methods

### Participants

An *a priori* power analysis, using data from a prior study, showed that ten participants were sufficient to identify strength differences of  $12.8 \pm 10.3$  Nm from a pilot study with a large effect size ( $d > 0.70$ ), with alpha level set at .05 and 90% power<sup>26</sup>. Thus ten individuals (Table 1) were recruited from the community and a rheumatology practice, and had a diagnosis of KOA with radiographic confirmation. Individuals with a history of knee surgery, intraarticular corticosteroid injection within 6 months, inability to walk without assistive devices, and any other neurological or muscular conditions affecting lower limb function were excluded from the study. In cases where participants had KOA in both knees, the involved limb was determined based on the knee with more severe symptoms. Before participating, all participants provided written informed consent approved by the university's institutional review board for biomedical sciences and participants' rights were protected.

### Procedure

Participants reported to the laboratory for a single session, wearing athletic clothing and shoes. Following providing written informed consent, participants completed a health history questionnaire, self-reported pain assessment using a visual analog scale (VAS) for both knees, and the knee osteoarthritis outcome score (KOOS) questionnaire<sup>27,28</sup>. After finishing the questionnaires, participants underwent a baseline assessment of concentric isokinetic and isometric hip strength and endurance using the Biodex System 4 Pro Dynamometer (Biodex Medical Systems Inc, Shirley, NY). Hip abduction was performed standing because it is the most appropriate physiological and functional position to compare to everyday activities and has good test-retest reliability<sup>29-31</sup>. Participants stood in a neutral position with the center of the dynamometer axis aligned with the anterior superior iliac

**Table 1.** Participant demographic and clinical characteristics at baseline (N = 10).

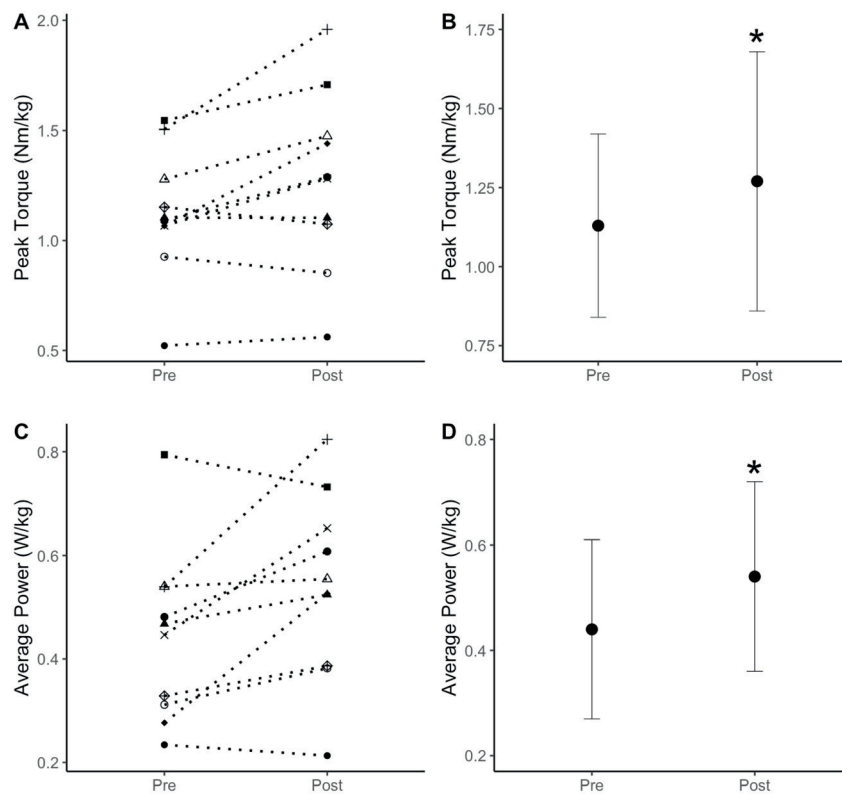
Demographic Variable	Mean $\pm$ Standard Deviation
Age (years)	68.70 $\pm$ 5.89
Sex (female), n (%)	4 (40%)
Height (m)	1.70 $\pm$ 0.10
Body Mass (kg)	84.40 $\pm$ 15.05
Body Mass Index (kg/m <sup>2</sup> )	28.93 $\pm$ 4.24
Affected/Involved Knee (right), n (%)	7 (70%)
KOOS – Symptoms	69.11 $\pm$ 17.46
KOOS – Pain	63.06 $\pm$ 12.43
KOOS – ADL	68.75 $\pm$ 16.84
KOOS – Sports/Recreation	36.50 $\pm$ 20.15
KOOS – QOL	48.13 $\pm$ 20.42

*Abbreviations: m, meters; kg, kilograms; ADL, activities of daily living; QOL, quality of life.*

spine (ASIS) of the side being tested<sup>15,19</sup>. Prior to testing, participants were allowed a brief warmup to familiarize themselves with the testing procedures. Subsequently, participants performed five repetitions of isokinetic hip abduction and adduction at 60 degrees/second with range of motion set from approximately 0 degrees to 30 degrees of hip abduction<sup>19,32</sup>. Verbal encouragement was provided throughout the repetitions.

Participants then completed isometric hip abductor strength and endurance testing while standing with their leg positioned and secured at 15 degrees of hip abduction<sup>19,32</sup>. Participants were instructed to maximally abduct the hip and sustain the isometric contraction for 30 seconds. Verbal encouragement was given only during the first five seconds of the isometric hold. Both isokinetic and isometric strength and endurance testing were completed on the involved limb first to allow for participants to adjust to the weight-bearing nature of the test, followed by assessments on the contralateral limb (uninvolved limb).

Following baseline hip abductor strength and endurance assessments, IC was administered on the involved leg in accordance with other studies that have used IC as an intervention<sup>24,33</sup>. IC was administered by the same member of the research team in a laboratory setting. A rapid inflation cuff (Hokanson SC12D cuff) was placed on the involved thigh while the patients were supine. The cuff was inflated to 225 mmHg for 5 minutes and then released for a 5-minute recovery period to allow for reperfusion. The cycle of inflation and reperfusion was repeated 5 times, for a total of 50 minutes<sup>24</sup>. Upon completion of IC, participants repeated the isokinetic and isometric standing hip abduction assessments of strength and endurance on the instrumented dynamometer, using the same protocols as previously described.



**Figure 1.** Changes in isokinetic measures, normalized to body mass, from pre- to post-IC in the involved limb. An asterisk indicates significantly different from pre-IC ( $p \leq 0.05$ ). A. Individual changes in isokinetic peak torque. Each symbol represents a separate participant. B. Group average with standard deviation of isokinetic peak torque pre- and post-IC. C. Individual changes in isokinetic average power. Each symbol represents a separate participant. D. Group average with standard deviation of isokinetic average power pre- and post-IC. Abbreviations: Nm, newton meter; kg, kilogram; W, watts.

### Data Analysis

Isokinetic peak torque, isokinetic average power, and isometric peak torque were normalized to mass. A fatigue index (FI) percentage was calculated for hip abduction endurance using the area under the force time curve ( $AUFC_{0-30}$ ) during the 30 second isometric contraction and the maximal torque generated during the first five seconds of the 30 second isometric contraction ( $F_{\max 0-5}$ ) as follows<sup>34</sup>:

$$FI (\%) = \left[ 1 - \frac{AUFC_{0-30}}{F_{\max 0-5} \times 30} \right] \times 100.$$

A lower fatigue index value was indicative of greater hip abductor endurance whereas a higher fatigue index value was indicative of reduced hip abductor endurance.

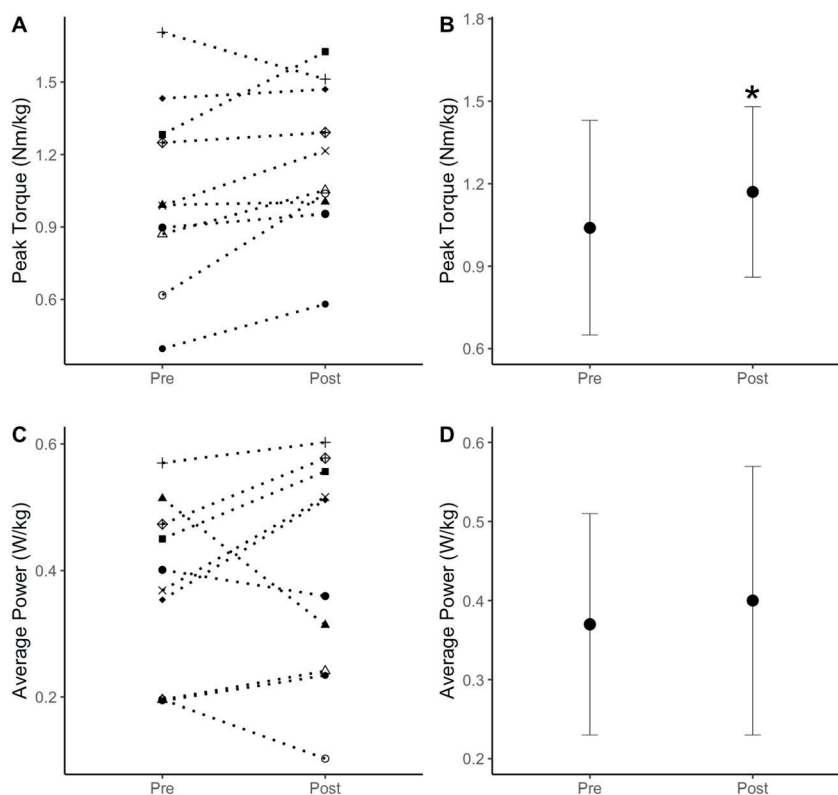
### Statistical Analysis

The Shapiro-Wilk test was used to verify normality of all outcome measures. Paired  $t$ -tests were used to determine

the changes in hip abductor strength, power, and endurance. Mean differences were calculated, and the magnitude of pre-post differences were estimated using Cohen's  $d$  effect sizes. Cohen's  $d$  effect sizes were interpreted as *weak* ( $<0.21$ ), *small* ( $0.21-0.39$ ), *medium* ( $0.4-0.69$ ), or *large* ( $\geq 0.7$ )<sup>35</sup>. Statistical significance for all analyses was set at  $p \leq 0.05$  *a priori*. All statistical analyses were performed in SPSS (version 28, IBM, Armonk, NY).

### Results

All variables were normally distributed based on the Shapiro-Wilk test ( $p > 0.05$ ). Isokinetic peak torque ( $p = 0.027$ ) and isokinetic average power ( $p = 0.025$ ) in the involved limb significantly increased after IC when compared to baseline (Figure 1). Isometric peak torque ( $p = 0.134$ ) and fatigue index ( $p = 0.769$ ) in the involved limb did not change significantly from pre- to post-IC (Table 2). In the uninvolved limb, isokinetic peak torque increased significantly after IC compared to baseline ( $p = 0.044$ ) (Figure 2). There were no significant



**Figure 2.** Changes in isokinetic measures, normalized to body mass, from pre- to post-IC in the uninvolved limb. An asterisk indicates significantly different from pre-IC ( $p \leq 0.05$ ). **A.** Individual changes in isokinetic peak torque. Each symbol represents a separate participant. **B.** Group average with standard deviation of isokinetic peak torque pre- and post-IC. **C.** Individual changes in isokinetic average power. Each symbol represents a separate participant. **D.** Group average with standard deviation of isokinetic average power pre- and post-IC. Abbreviations: Nm, newton meter; kg, kilogram; W, watts.

changes in isokinetic average power ( $p=0.424$ ) (Figure 2), isometric peak torque ( $p=0.369$ ), or fatigue index ( $p=0.267$ ) in the uninvolved limb from pre- to post-IC (Table 3). Effect sizes for the outcome measures on both limbs ranged from weak to medium (Tables 2 and 3).

## Discussion

The purpose of this study was to investigate the effect of a single session of IC on hip abductor strength in participants with symptomatic KOA. Participants demonstrated increased strength, as evidenced by greater peak torque and average power in the involved limb, with an average 12.39% increase in isokinetic peak torque. This is comparable to other studies that have reported a 11.1% increase in isometric hip abductor strength after a 12-week hip abductor strengthening program<sup>36</sup> and 15.5% increase in isokinetic hip abductor strength after a 6-week intensive hip abductor strengthening program<sup>37</sup>. Follow-up measurements in the second study reported that subjects maintained this strength increase

through the 12<sup>th</sup> week, reporting a 12.9% increase in hip abductor strength from baseline measured 6 weeks after completion of the strengthening program<sup>37</sup>. The strength increase reported at week 12 following the 6 week strengthening program is very comparable to the 12.39% increase in hip abductor strength seen in the current study, possible after only a single session of IC. This suggests that a single session of IC may be as beneficial as some strengthening programs, but further research needs to be completed comparing the two interventions in this population.

The results also partially supported our secondary hypothesis showing significant increases in isokinetic hip abductor strength in the uninvolved limb after IC which was similar to other studies that have reported systemic effects of IC<sup>25</sup>. The systemic effect of IC can improve hip abductor strength in both limbs in individuals with KOA which could potentially address some of the compensatory behaviors employed in the contralateral (uninvolved) limb in this population. Increased hip strength can potentially improve pelvic control allowing for more trunk stability during

**Table 2.** Average strength and endurance measures at baseline and post IC and changes in outcome measures reported as mean differences and effect sizes in the involved limb.

Outcome Measure	Pre IC	Post IC	Mean Difference	Effect Size
Isokinetic Peak Torque (Nm/kg)	1.13 (0.29)	1.27 (0.41)*	0.15	0.42
Isokinetic Average Power (W/kg)	0.44 (0.17)	0.54 (0.18)*	0.10	0.57
Isometric Peak Torque (Nm/kg)	0.97 (0.35)	1.07 (0.24)	0.10	0.33
Fatigue Index (%)	21.19 (5.41)	20.32 (6.16)	-0.87	-0.15

*Abbreviations: Nm, newton meter; kg, kilogram; W, watts. Values are reported as mean (SD). \*Indicates significant increase from baseline.*

**Table 3.** Average strength and endurance measures at baseline and post IC and changes in outcome measures reported as mean differences and effect sizes in the uninvolved limb.

Outcome Measure	Pre IC	Post IC	Mean Difference	Effect Size
Isokinetic Peak Torque (Nm/kg)	1.04 (0.39)	1.17 (0.31)*	0.13	0.37
Isokinetic Average Power (W/kg)	0.37 (0.14)	0.40 (0.17)	0.03	0.19
Isometric Peak Torque (Nm/kg)	0.94 (0.24)	0.98 (0.31)	0.04	0.14
Fatigue Index (%)	24.85 (8.17)	21.12 (4.94)	-3.73	-0.55

*Abbreviations: Nm, newton meter; kg, kilogram; W, watts. Values are reported as mean (SD). \*Indicates significant increase from baseline.*

gait<sup>36</sup>. Hip strengthening exercises can also have functional implications, such as improved walking distance, improved performance on the sit to stand test, and reduced symptoms and pain, which leads to improved quality of life<sup>19,36,38</sup>. The use of IC as a noninvasive intervention to potentially reduce knee pain and improve mechanics may allow patients with KOA to remain active, which can be the first step to breaking the vicious cycle that leads to inactivity in this population. Therefore, IC may be an effective intervention to improve quality of life in persons with KOA.

Although there were changes in strength and power, there were no significant changes in hip endurance in either limb. Hip endurance is particularly important for patients with KOA because these patients have a high risk of developing secondary joint disorders, such as hip OA and low back pain. Lack of endurance in the hip musculature can increase compensatory behaviors involving the low back muscles, and allow for load transfer, thereby increasing comorbidity<sup>39</sup>. Decreased hip muscle endurance can thus lead to a pain avoidance behavior which can cause low back muscle weakness and chronic low back pain<sup>39</sup>. Reduced endurance can potentially also have implications on balance in patients with KOA. A single session of IC, although beneficial to strength, may induce temporary priming effects of muscles due to increased oxygenation and reperfusion. Perhaps chronic exposure to repeated cycles of ischemia and reperfusion is necessary to see endurance effects.

There could be many mechanisms that led to the increase in strength, such as physiological changes and temporary

hypertrophy of the hip abductors. Hypertrophy from muscle ischemia has been previously observed from the metabolic stress induced during ischemia which leads to the accumulation of metabolites<sup>40</sup>. Combined with increased oxygenation and rate of deoxygenation of the hemoglobin and myoglobin during the reperfusion phase of IC, it is possible that type II muscle fibers benefited more from IC because of their lower microvascular oxygen partial pressure<sup>22</sup>. Furthermore, ischemia leads to increased activation of type II fibers after chronic IC, however it is unknown if these changes are just temporary and whether similar effects are seen after acute IC in individuals with KOA<sup>41,42</sup>. Future work in this area may consider the use of a muscle biopsy to confirm these physiologic changes in muscle fibers and evaluate whether acute IC can have lasting hypertrophy effects.

Another potential mechanism for the strength and power increases following IC could be attributed to neural adaptation, resulting in an engaged and overactive autonomic nervous system. IC has been shown to activate the group III and group IV afferents, which are sensitive to ischemia, leading to the release of neuromodulators such as serotonin and norepinephrine from the brain stem centers<sup>43,44</sup>. These neuromodulators increase the excitability of spinal motoneurons and potentially the excitability of weaker muscles<sup>45</sup>. Increased activation of atrophied hip abductors in KOA patients could contribute to the observed increase in strength. Our data also suggests a potential systemic effect of IC based on the increase in peak torque observed in the uninvolved limb. Other studies have reported similar systemic



effects<sup>46</sup> which could be an adaptation of the nervous system to ischemia<sup>44</sup>.

Despite the mechanism for improved strength, IC may be a useful intervention in conjunction with physical therapy as a pre-therapy agent, allowing patients to be more functionally mobile for their sessions. This can help patients get more benefits from their physical therapy sessions and complete exercises with reduced pain. Further, IC may help improve pain-related non-adherence to exercise and prescribed walking, and can help keep this population motivated. Overall, IC, when used in conjunction with other treatment options, can help alleviate several barriers that limit persons with KOA from existing treatment options, and improve their functional mobility, gait, and overall quality of life.

### Limitations

There were some limitations in the current study. First, our study sample consisted mostly of men (60%), which may not accurately represent the incidence and prevalence of KOA in women, or their associated severity in the population<sup>47</sup>. Typically, the incidence of KOA is about 1.5 to 2 times higher in women than in men and women also exhibit greater KOA severity<sup>47-49</sup>. Response to IC based on sex differences is currently unknown. Future studies should consider sex differences in the response to IC in persons with KOA.

Second, we did not control for the severity in KOA, which may have affected the response to IC. As the first study to explore the use of IC to improve hip strength in this population, we included a wider range of participants with symptomatic KOA rather than limit participation based on a Kellgren and Lawrence grade. Future studies should confirm KOA severity and determine if the effects of IC vary with KOA severity and exercise history.

### Conclusion

A single session of IC increased hip abductor isokinetic peak torque in the involved and uninvolved limbs, and isokinetic average power in the involved limb. The increased strength and power after IC can be beneficial to KOA patients by improving pain related physical function and mobility, and thereby increasing their quality of life. These changes can potentially improve pain related non-adherence to other treatment options like prescribed walking and allow for better outcomes from strengthening and physical therapy sessions. Clinicians and clinical researchers may consider the use of IC as a passive, non-invasive, accompanying modality to help with muscle strength and as a treatment option for patients with KOA.

### Ethics approval

The study protocol was approved by the Institutional Review Board at the University of Illinois at Chicago on January 25, 2023 (IRB # 2022-1600).

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### Authors' Contributions

SS was responsible for IRB submission, study conception and design, participant recruitment, data collection and analysis, and manuscript preparation and revision. KCF was responsible for assisting with data analysis and manuscript preparation and revision. PJ was responsible for participant recruitment and manuscript preparation and revision. LSH provided oversight over IRB submission, study conception and design, data collection and analysis, and was responsible for manuscript preparation and revision.

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