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Differences in muscle strength after ACL reconstruction do not influence cardiorespiratory responses to isometabolic exercise

Marília S. Andrade¹, Claudio A. B. Lira², Rodrigo L. Vancini³,
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ABSTRACT | Objectives: To investigate whether the muscle strength decrease that follows anterior cruciate ligament (ACL) reconstruction would lead to different cardiorespiratory adjustments during dynamic exercise. **Method:** Eighteen active male subjects were submitted to isokinetic evaluation of knee flexor and extensor muscles four months after ACL surgery. Thigh circumference was also measured and an incremental unilateral cardiopulmonary exercise test was performed separately for both involved and uninvolved lower limbs in order to compare heart rate, oxygen consumption, minute ventilation, and ventilatory pattern (breath rate, tidal volume, inspiratory time, expiratory time, tidal volume/inspiratory time) at three different workloads (moderate, anaerobic threshold, and maximal). **Results:** There was a significant difference between isokinetic extensor peak torque measured in the involved (116.5 ± 29.1 Nm) and uninvolved (220.8 ± 40.4 Nm) limbs, $p=0.000$. Isokinetic flexor peak torque was also lower in the involved limb than in the uninvolved limb (107.8 ± 15.4 and 132.5 ± 26.3 Nm, $p=0.004$, respectively). Lower values were also found in involved thigh circumference as compared with uninvolved limb (46.9 ± 4.3 and 48.5 ± 3.9 cm, $p=0.005$, respectively). No differences were found between the lower limbs in any of the variables of the incremental cardiopulmonary tests at all exercise intensities. **Conclusions:** Our findings indicate that, four months after ACL surgery, there is a significant deficit in isokinetic strength in the involved limb, but these differences in muscle strength requirement do not produce differences in the cardiorespiratory adjustments to exercise. Based on the hypotheses from the literature which explain the differences in the physiological responses to exercise for different muscle masses, we can deduce that, after 4 months of a rehabilitation program after an ACL reconstruction, individuals probably do not present differences in muscle oxidative and peripheral perfusion capacities that could elicit higher levels of peripheral cardiorespiratory stimulus during exercise. **Keywords:** rehabilitation; anterior cruciate ligament; isokinetic testing; physical therapy; oxygen uptake; ventilatory response.

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● Introduction

The maintenance of homeostasis during exercise requires different physiological adjustments. The final response to moderate exercise is characterized by a steady state of physiological variables¹. The physiological variables in the steady state of exercise tend to match the metabolic rate while the respiratory exchange ratio and the partial arterial pressures of carbon dioxide and oxygen remain close to resting levels². Blood lactate concentration also remains near resting values during the steady state of moderate exercise². Consequently, minute ventilation (\dot{V}_E) is proportional to oxygen uptake ($\dot{V}O_2$) and carbon dioxide production ($\dot{V}CO_2$)¹. In the same way as

\dot{V}_E , cardiovascular responses also adapt to exercise intensity under the command of the autonomic nervous system¹.

Under certain conditions, however, the proportionality between ventilatory and cardiovascular responses to exercise intensity is lost. For instance, exercise performed by different muscle masses at the same level of $\dot{V}O_2$ leads to significantly higher \dot{V}_E and heart rate (HR) for a smaller muscle mass^{2,3}. In the attempt to explain such findings, different hypotheses were formulated to elucidate the cardiorespiratory control during exercise, namely central command, peripheral chemoreceptors, and spinal reflexes⁴.

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According to the central command hypothesis, the changes in cardiorespiratory variables that occur during exercise may be partly explained by the 'radiation' of activity in central neurons innervating exercising muscles to the respiratory and cardiovascular control areas³, serving as a feed-forward control mechanism that provides an adequate ventilatory response to the metabolic demands of exercise⁵. Cardiorespiratory and locomotor responses are proportional, and only a fine adjustment feedback system (via humoral or peripheral neurogenic mechanisms) is necessary to assure an adequate ventilatory response to the metabolic demands of exercise. Several authors have suggested that central command is responsible for the ventilatory control in different types of exercise with different muscle mass, such as in subjects with unilateral atrophy³, pharmacologically induced paralysis⁶ or during imagination of exercise without performing it⁷. In all these models there is a strong correlation between ventilatory response and the level of central command.

The chemoreceptor hypothesis (aortic and carotid bodies) has been supported, especially for hyperpnea related to exercise when there is metabolic acidosis⁸. Several different stimuli may be responsible for increasing the contribution of the peripheral chemoreceptors to ventilation during exercise, as long as a degree of hypoxia is present⁹. In relation to the spinal reflex theory, peripheral neurogenic stimuli originated in receptors located inside or outside the exercising muscles are related to the perception of muscle movement, position of the joints, muscular metabolic changes and changes in vascular conductance of exercising muscles^{1,4,9}. Different authors have proposed that exaggerated cardiorespiratory response in relation to the metabolic demand observed during exercise with different muscle masses is determined by intramuscular metabolic receptors sensitive to local metabolic changes in the same absolute workload, exercise performed with a smaller muscle mass produces more intense metabolic responses^{2,10}. Others suggest that cardiorespiratory control is not correlated with the local metabolic changes, but with variation in peripheral blood flow, obstruction of venous flow for exercising muscles increases the ventilatory response and when the arterial flow is also blocked the ventilatory response diminishes, indicating that local vascular conductance plays an important role in the ventilatory adjustments to exercise¹¹.

Regardless of the mechanisms that could explain higher cardiorespiratory responses to exercise

performed by smaller muscle masses, the knowledge of these differences may be useful in orthopedic rehabilitation procedures. In clinical practice, a common situation that results in muscular (strength, power, and endurance) and sensory deficits is anterior cruciate ligament (ACL) reconstruction¹². After surgery, the patient presents a significant loss in muscle strength, especially in the quadriceps muscle, even 6 months after ACL reconstruction^{13,14}. To identify successful outcomes after surgery, members of several international sports medicine associations (American Orthopedic Society for Sports Medicine, the European Society for Sports Traumatology, Surgery, and Knee Arthroscopy, and the American Physical Therapy Association) agree with the following criteria: thigh muscle strength recovery (strength level greater than 90% of the uninjured limb), absence of giving way, return to sports, no more than mild knee joint effusion, and using patient-reported outcomes. Therefore, given that patients who were submitted to ACL reconstruction presented significantly smaller thigh mass, it is possible that they presented higher cardiorespiratory responses to isometabolic unilateral exercise during the process of rehabilitation to recover lower limb muscle mass. If so, these differences may be used as criteria to infer the extent of muscular deficiency and to guide orthopedic and sports rehabilitation procedures. Previous studies have demonstrated differences in cardiorespiratory responses to isometabolic exercise performed by different muscle masses^{15,16}, however these studies are from the 1990s and there are no studies comparing lower limb responses after unilateral ligament reconstruction.

Thus, the aim of the study was to verify whether there are differences in cardiorespiratory adjustments to dynamic exercise performed by both uninvolved and involved lower limbs after unilateral ACL reconstruction. We hypothesized that, due to differences in muscle mass, cardiorespiratory adjustments to dynamic exercise are exacerbated when both involved and uninvolved limbs results are compared.

• Method

Subjects

Eighteen physically active male subjects (2.7 ± 0.7 hours/week of physical activity) participated in the study. Their mean age was 33 ± 12 years, height was 177 ± 5 cm, and body mass was 79 ± 9 kg.

Subjects were submitted to intra-articular ACL reconstruction with patellar tendon graft performed by the same surgical team. Following the surgery, they participated in a standardized ACL rehabilitation program for both limbs, as previously described by Carey et al.¹⁷. Sessions were held three times a week. In addition to cruciate ligament tear, the lateral meniscus was involved in four subjects, the medial meniscus in seven subjects, and both lateral and medial menisci in one subject.

The subjects were informed about the purpose of the research and were asked to give their written consent to participate in the protocol approved by the Ethics Committee of Universidade Federal de São Paulo (UNIFESP), São Paulo, SP, Brazil (protocol 281/99). All experimental procedures were in accordance with the recommendations of the Declaration of Helsinki.

Experimental procedures

The entire evaluation lasted two consecutive days, starting four months after the surgery. This time period was chosen in order to minimize the possibility of pain or fear, which could influence the physiological responses to exercise and be harmful to the integrity of the graft. On the first day, the volunteers were submitted to isokinetic muscular evaluation of the knee flexor and extensor muscles. Measurement of the thigh circumference was taken and the knee range of motion (ROM) was assessed in order to verify the losses in muscular function caused by surgery. Thigh circumference and ROM were performed in a random order before the isokinetic test. Evaluation of the cardiorespiratory responses to exercise for both limbs (involved and uninvolved) was performed on the second day.

Isokinetic muscle test. Before isokinetic testing, a 5-min warm-up was performed on a cycle ergometer (Cybex Inc., Ronkonkoma, NY, USA) at a resistance level of 25 W followed by low-intensity dynamic stretching exercises for the hamstrings and quadriceps stretching exercises¹⁸. Following the warm-up, subjects were placed on the isokinetic dynamometer (Cybex – division of Lumex, Cybex 6000) to assess the concentric strength measurements for both involved and uninvolved lower limbs. Subjects assumed a seated position on the isokinetic dynamometer with their hips flexed at approximately 85 deg, measured by the scale in the isokinetic dynamometer chair. Standard stabilization straps were placed across the trunk, the waist, and the distal femur of the tested limb to minimize additional movement and to provide the same conditions for all participants.

The axis of the dynamometer was visually aligned with the lateral femoral condyle while the knees were flexed at 90 deg. The length of the lever arm was individually determined by the length of each individual's lower leg, and the resistance pad was placed proximal to the medial malleolus. Following the direct measurement at 30 deg of knee extension, gravity correction procedures were applied according to the manufacturer's specifications to reduce the risk of inaccurate data. The knee flexion/extension range of motion was standardized from 5 to 95 deg, with full knee extension referenced as being 0 deg, following previous procedures¹⁸. Given that maximal torque output is not altered by small variations in range of motion during isokinetic activity testing¹⁸, this range of motion was chosen to prevent graft injury. The sequence of sides for each subject was randomized and all participants were tested on extension first.

As part of the familiarization process, the participants were given standard verbal instructions regarding the procedures and were allowed a few (no more than 5) sub-maximal practice attempts for each test condition. After 1 minute, the subjects were tested with a maximum of 5 repetitions performed at 60°/s, with no rest period between knee extension and flexion assessments, and the results were recorded for analysis. This number of repetitions has been shown to have high reliability for isokinetic testing¹⁹. Consistent verbal commands were given by the examiner during each test to ensure maximal effort, and visual feedback of the recorded torque was provided during the test. All subjects were tested by the same examiner who was trained and experienced in the use of isokinetic testing devices. The evaluated parameters were peak torque (in Nm), total work (in Joules), and set total work (in Joules) of the hamstrings and quadriceps. Contralateral deficits (in %) [$1 - (\text{involved limb value} / \text{uninvolved limb value}) * 100$] were calculated for all three variables measured and for both flexor and extensor muscles.

Thigh circumference

Thigh circumference was taken with a tape measure 10 cm above the superior pole of the patella, with the subject in a standing position and both feet on the floor.

Knee range of motion

Knee flexion and extension ROM in degrees were measured bilaterally in prone. For this purpose, the lateral femoral condyle was used as a landmark for the measurement of knee flexion and extension. The central pivot of a universal goniometer (CARCI, São

Paulo, SP, Brazil) was placed over the midpoint of the lateral joint margin, with the stationary arm aligned with the great trochanter. The moving arm was then aligned with the lateral malleolus with the neutral position taken as zero. To measure knee flexion, the hip was initially at 0 deg of extension, abduction, and adduction. In order to avoid knee flexion, the examiner held the lower limb and stabilized the femur to prevent hip rotation, abduction or adduction. To measure knee extension, the lower limb was extended. The previous precautions were taken to prevent compensations (i.e. adduction, abduction, and rotation). Measurements were carried out by a single experienced examiner.

Cardiopulmonary incremental exercise test

The comparative study between the limbs was performed using an isokinetic dynamometer Cybex 6000 in the isotonic mode. For this purpose, a special test was designed to measure the cardiorespiratory responses to exercise in closed kinetic chain, similar to the rehabilitation exercises. An adaptation in the equipment was done to allow extremity fixation to the lever system in closed kinetic chain (Figure 1). The subjects were kept in supine and performed active triple extension (ankle, knee, and hip), while flexion was passive. The protocol consisted of an initial workload of 15% of the involved limb, maximal isokinetic knee extensor peak torque (open kinetic chain) (mean = 21.6 Nm and SD=7.4 Nm) for both limbs, with 10% increments every minute until volitional exhaustion, with a cadence of 45 cycles per minute guided by a metronome. Total test time was approximately 8 to 10 minutes for each limb. The test protocol was the same for both limbs to ensure that involved and uninvolved limbs were tested with

identical workloads. All subjects received a 60-min rest period between tests to prevent the build-up of fatigue. The sequence of lower limbs for each subject was randomized. During the test, subjects breathed through a two-way valve and the exhaled air was analyzed by a breath-by-breath metabolic system (Vmax 229, Sensor Medics, USA). The metabolic system was calibrated before each test according to the manufacturer's recommendations. HR was measured with a heart rate monitor (Vantage, Polar, Finland). For the purposes of the present study, the outcomes of interest were $\dot{V}O_2$, \dot{V}_E , ventilatory equivalent for O_2 ($\dot{V}_E/\dot{V}O_2$), ventilatory equivalent for CO_2 ($\dot{V}_E/\dot{V}CO_2$), end-tidal pressure of O_2 (PETO₂), end-tidal pressure of CO_2 (PETCO₂), inspiration time (Ti), expiration time (Te), tidal volume (V_T), respiratory drive (V_T/Ti), breathing rate (f), and HR. The anaerobic ventilatory threshold was indirectly estimated from breath-by-breath responses as the $\dot{V}O_2$ at which PETO₂ and the $\dot{V}_E/\dot{V}O_2$ systematically began to increase without simultaneous increase in the $\dot{V}_E/\dot{V}CO_2$ and decrease in PETCO₂⁸.

Statistical analysis

Sample size calculation was performed considering the type one error ($\alpha=0.05$) and the type two error ($\beta=0.20$). The calculations indicated that a sample of 16 subjects would be necessary to identify significant differences in minute ventilation. The results are expressed as mean (SD). As variables presented normal distributions according to the Shapiro-Wilk test, we used the paired Student t-test to compare the values for both limbs. The level of significance was set at $p<0.05$. All statistical analyses were performed with Statistica, version 7.0 (Statsoft Inc, Tulsa, Oklahoma, USA).

Results

Four months after ACL surgery the involved limb was impaired when compared with the uninvolved limb for all measured muscle variables: thigh circumference (−3.3%), range of motion (−2.4%), isokinetic extensor peak torque (−47.2%), isokinetic extensor total work (−43.0%), isokinetic flexor peak torque (−12.7%), and isokinetic flexor total work (−11.5%) (Table 1).

All variables analyzed in the cardiopulmonary exercise incremental test ($\dot{V}O_2$, \dot{V}_E , $\dot{V}_E/\dot{V}O_2$, Ti, Te, V_T , V_T/Ti , f , HR, and workload) were similar for both limbs at each of the different exercise intensities (moderate, anaerobic threshold workload, and peak effort) (Table 2).



Figure 1. Cardiopulmonary incremental exercise test performed on isokinetic device.

Table 1. Muscle characteristics obtained from involved and uninvolved limbs four months after anterior cruciate ligament reconstruction surgery.

	Involved		Uninvolved		p value	d value
	Mean	SD	Mean	SD		
Thigh circumference (cm)	46.9	4.3	48.5	3.9	0.005	0.38
Range of motion (degrees)	126.1	5.2	129.3	5.5	0.01	0.59
Knee extensor peak torque (Nm)	116.5	29.1	220.8	40.4	0.00000	2.9
Knee extensor total work (J)	135.2	31.2	237.5	57.1	0.00001	2.22
Knee flexor peak torque (Nm)	107.8	15.4	123.5	26.3	0.004	0.72
Knee flexor total work (J)	129.5	24.7	146.3	36.7	0.01	0.53

Table 2. Cardiorespiratory responses to unilateral exercise test for the involved and uninvolved limbs during moderate, anaerobic threshold (AnT), and peak effort.

	HR		$\dot{V}O_2$		VE		$\dot{V}E/\dot{V}O_2$		f		V_T		Ti		Te		V_T/Ti	
	beats.min ⁻¹		L.min ⁻¹		L.min ⁻¹				bpm		L		s		s		L.s ⁻¹	
Moderate	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Uninvolved	90	14	0.58	0.25	18.9	5.4	37	14	27	5	0.7	0.1	1.1	0.3	1.2	0.3	0.7	0.2
Involved	88	12	0.57	0.20	18.4	5.1	36	13	29	7	0.7	0.2	1.1	0.3	1.2	0.3	0.7	0.2
AnT																		
Uninvolved	105	16	0.98	0.34	26.4	5.5	27	6	27	6	1.0	0.3	1.1	0.3	1.2	0.3	0.9	0.2
Involved	104	14	0.96	0.22	25.6	5.1	27	6	29	4	1.0	0.3	1.2	0.5	1.1	0.2	0.9	0.2
Peak																		
Uninvolved	141	21	1.75	0.45	63.6	19.6	37	8	41	11	1.6	0.4	0.9	0.3	0.7	0.2	2.0	0.7
Involved	137	21	1.81	0.47	62.1	17.9	35	8	41	10	1.6	0.6	0.8	0.2	0.7	0.2	1.9	0.5

HR: heart rate; $\dot{V}O_2$: oxygen consumption; VE: minute ventilation; f: breath rate; V_T : tidal volume; Ti: inspiratory time; Te: expiratory time; V_T/Ti : tidal volume/inspiratory time.

● Discussion

This is the first study to examine the effects of ACL reconstruction surgery on cardiorespiratory responses to isometabolic exercise performed unilaterally. We found that, despite prominent impairment to muscle function (i.e. decrease in isokinetic muscle strength in involved limb compared with uninvolved limb), the cardiorespiratory responses to exercise were similar. This is a novel result because previous studies that investigated the effects of different muscle masses on physiological responses to exercise (one vs. two leg exercise¹⁵, upper vs. lower limb exercise¹⁶, and systemic illnesses that affect muscle mass such as chronic heart failure¹⁰) found that smaller muscle masses present more exacerbated physiological responses to isometabolic exercise.

In the present study on muscle function four months after ACL reconstruction, the involved limb presented a smaller thigh circumference than the uninvolved limb due to the muscle atrophy process after ligament reconstruction that resulted in a

decrease in muscle work capacity and contraction, thus leading to lower values for knee extensor and flexor isokinetic torque.

In fact, quadriceps hypotrophy is a phenomenon expected in patients in the postoperative phase of ACL reconstruction, and higher deficit levels were expected after ACL reconstruction with patellar tendon than ACL reconstruction with hamstring graft, even though no difference was found between the two surgical procedures (patellar tendon graft or hamstring graft) over two years after surgery²⁰. Concerning studies including quadriceps strength measurements, some authors showed that the contralateral deficit between limbs can still be seen up to two years after surgery²¹. Nevertheless, this strength deficit seems to have no correlation with other variables such as functional level and residual ligament laxity, indicating a lack of evidence of direct dependence on muscle response²¹. Similarly, our study did not find dependence between muscle impairment due to ACL reconstruction surgery and physiological responses to exercise.

Long periods of skeletal muscle inactivity (due to limb immobilization, bed rest, physical inactivity or space flight) result in a myriad of physiological adaptations in skeletal muscle form and function that clinically manifest themselves as losses in muscle performance and require time-consuming physical rehabilitation²². In this context, immobilization is a model widely used to study skeletal muscle wasting that causes similar muscle repercussion to that of ACL reconstruction.

Skeletal muscle hypotrophy can occur due to a decrease in protein synthesis, an increase in the rate of protein degradation or a combination of both increased proteolysis and depressed protein synthesis. In animal models of disuse atrophy, it has been shown that inactivity-induced muscle hypotrophy occurs due to a decrease in protein synthesis and an increase in the rate of proteolysis²³. In the hindlimb suspension model of skeletal muscle atrophy, the rate of protein synthesis declines rapidly following the onset of muscle unloading. This decrease in muscle protein synthesis reaches a new steady-state level at roughly 48 hours²³. Further, the reduction in protein synthesis is followed by a large and rapid increase in proteolysis mediated by several key proteases.

Moreover, skeletal muscle atrophy and weakness can occur due to neurological and skeletal muscle impaired properties, as it is well known that the output from these sources controls voluntary force production²⁴. Concerning the nervous system for instance, Seki et al.²⁵ reported that the mean firing rate of the motor neuron in the first dorsal interosseous during maximal voluntary contraction decreased 15% after 1 week of finger immobilization. It is likely that the relative contribution of neural and muscular factors dynamically changes over time, with the muscular component contributing more as the duration of disuse increases²⁶. Therefore, the muscle wasting after ACL reconstruction surgery can be attributed to the abovementioned aspects.

Because skeletal muscle is a plastic tissue that responds to increased or decreased contractile activity after ACL reconstruction surgery, its spontaneous recovery process can be amplified by rehabilitation. In an animal model study, Desplanches et al.²⁷ compared the effects of spontaneous recovery and treadmill retraining for 8 weeks on $\dot{V}O_{2\max}$, histochemical, and biochemical muscular properties. The rats were submitted to 5 weeks of hindlimb suspension. The authors found that spontaneous recovery reversed 15% of the decrease in $\dot{V}O_{2\max}$, whereas retraining induced a 20% rise above control values. In the spontaneous recovery group, both citrate synthase and 3-hydroxyacyl-CoA dehydrogenase activities,

decreased by hypokinesia (–40%), increased but remained 20% below the control level, respectively. In the post-hypokinesia training group, there was a rise in these activities above control values (+50 and +20%, respectively).

Recovery or training led to 100% distribution of type I fiber in the soleus muscle and to a full recovery of all fiber cross-sectional areas. In the spontaneous recovery group, the amount of capillaries per fiber decreased by 46%, returning to the normal range. In the post-hypokinesia group, training induced a rise in the capillaries per fiber above their control values (+23%). These results point to the plasticity of the muscle and indicate the need of a post-hypokinesia training program for the full recovery of oxidative enzyme capacity.

In another study, Witzmann et al.²⁸ studied contractile properties in rats remobilized after 6 weeks of hindlimb immobilization to evaluate the regenerative capacity of fast and slow skeletal muscle. The authors found that slow skeletal muscle was more sensitive to immobilization. However, its recovery rate was greater, occurring earlier than the fast muscle recovery. According to the authors, this is probably the result of higher protein turnover rates in slow skeletal muscle.

Therefore, this can be a possible explanation for our results. As the cardiorespiratory responses to exercise evaluated by the present study are related to aerobic metabolism, it is possible that oxidative status recovery (i.e. oxidative metabolism enzymes recovery) had happened earlier. In addition, during the first months of the rehabilitation process after ACL surgery, the patient needs to avoid heavy weight exercises, because it may be harmful to the new ligament graft and it may create an inflammatory process in the weakened quadriceps tendon. This type of exercise, particularly eccentric contraction²⁹, has been shown to increase strength recovery but it was not emphasized in the first months after surgery. Therefore, it is possible that the oxidative status recovery had occurred before the strength status recovery. Likewise, fast skeletal muscle did not recover completely, which would explain the differences related to muscle strength.

● Limitations

In this study, we showed that there was no difference in cardiorespiratory responses to isometric exercise after a 4-month rehabilitation program post-ACL reconstruction because of the significant loss in strength in the involved lower

limb. However, this study was designed to begin evaluations 4 months after surgery, and future studies with earlier evaluations could show significant cardiorespiratory differences that may be useful in the rehabilitation process. Another possible limitation of this study was the fact that the strength evaluation was done in an open kinetic chain and the muscles involved in the test were only the knee flexors and extensors. On the other hand, in the cardiopulmonary incremental exercise test all lower limb muscles were involved as it was done in a closed kinetic chain. It is possible that the strength deficit of the extensor muscles was minimized in the cardiopulmonary incremental exercise test by the other muscular actions.

Clinical implications

After 4 months of rehabilitation post-ACL reconstruction, there are no differences in cardiorespiratory adjustments to dynamic exercise performed by both uninvolved and involved lower limbs after unilateral ACL reconstruction. The limb muscles may not present differences in oxidative and peripheral perfusion capacities that could elicit higher levels of peripheral cardiorespiratory stimulus during exercise because of the significant weakness of the knee extensor muscles. These results can be useful to guide the rehabilitation program for this very common knee ligament injury in orthopedic and sports settings.

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