**UNIVERSIDADE FEDERAL DE SÃO CARLOS**
**CENTRO DE CIÊNCIAS BIOLÓGICAS E DA SAÚDE (CCBS)**
**PROGRAMA DE PÓS-GRADUAÇÃO EM FISIOTERAPIA**

# Efeitos Imediatos da Crioterapia sobre o Desempenho Neuromuscular da Articulação do Tornozelo e o Padrão da Marcha de Indivíduos Hemiparéticos Espásticos Crônicos Pós-AVE

**CAROLINA CARMONA DE ALCÂNTARA**

**SÃO CARLOS**
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**CAROLINA CARMONA DE ALCÂNTARA**

Tese apresentada ao Programa de Pós-Graduação em Fisioterapia da Universidade Federal de São Carlos, como parte dos requisitos para a obtenção do Título de Doutor em Fisioterapia.

**Orientador:** Prof. Dr. Thiago Luiz de Russo

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Programa de Pós-Graduação em Fisioterapia

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# RESUMO

**Introdução:** O Acidente Vascular Encefálico (AVE) tem sido descrito como a terceira causa de morte e principal causa de incapacidade na população adulta mundial. Déficits nas funções dos membros inferiores frequentemente persistem na grande maioria dos casos, afetando a marcha e a mobilidade funcional. Neste âmbito, diversas intervenções são aplicadas na prática clínica para otimizar o desempenho funcional. A crioterapia está entre as técnicas utilizadas no intuito de reduzir temporariamente a espasticidade, permitindo a realização de treinos funcionais, como a marcha. No entanto, seus efeitos sobre o tônus muscular, o desempenho muscular e o padrão da marcha de indivíduos com hemiparesia crônica ainda não estão elucidados. **Objetivos:** Avaliar os efeitos imediatos da crioterapia (pacote de gelo) sobre o tônus muscular, o torque isométrico e isocinético dos músculos dorsiflexores e flexores plantares, e sobre parâmetros angulares e espaço-temporais da marcha em indivíduos hemiparéticos espásticos crônicos. **Métodos:** *Desenho experimental:* estudo crossover randomizado controlado. *Participantes:* Dezesseis sujeitos hemiparéticos crônicos. *Intervenção:* Crioterapia (pacote de gelo) ou Intervenção Controle (pacote de areia à temperatura ambiente) aplicado sobre os músculos flexores plantares do membro parético. *Avaliações (pré/pós intervenção):* 1) Tônus muscular, de acordo com a Escala de Ashworth modificada; 2) Cinemática espaço-temporal e angular do quadril, joelho e tornozelo (flexão / extensão) durante a marcha obtida por meio de um sistema de análise de movimento tridimensional (Qualisys); 3) Torque isométrico, concêntrico e excêntrico de dorsiflexão e flexãoplantar, avaliados em dinamômetro isocinético. *Análise estatística:* O teste ANOVA two-way de medidas repetidas foi utilizado para análise de todas as variáveis cinemáticas e de torque muscular. Os testes não paramétricos de Wilcoxon e Mann-Whitney foram utilizados para comparações da pontuação na EAM, por ser considerada uma variável categórica. Um nível de significância de 0,05 foi considerado para todos os testes estatísticos. **Resultados:** A crioterapia reduziu o tônus dos flexores plantares, mas não alterou a capacidade de geração de torque e parâmetros espaço-temporais ou angulares (plano sagital) durante a marcha em comparação com a intervenção controle. **Conclusão:** Os achados deste estudo sugerem que a crioterapia (pacote de gelo) aplicada sobre os músculos flexores plantares indivíduos com hemiparesia crônica parece ser uma técnica eficaz para reduzir o tônus muscular, mensurado clinicamente, mas não afeta o desempenho muscular e o padrão de marcha destes indivíduos.


**Palavras-chave:** Espasticidade, Marcha, Cinemática, Força muscular, Crioterapia, AVE.

## ABSTRACT

**Introduction:** Stroke has been described as the third leading cause of death and the leading cause of disability in the adult population worldwide. Deficits in lower limb functions often persist in the vast majority of cases, affecting gait and functional mobility. In this context, several interventions are applied in the clinical practice to optimize functional performance. Cryotherapy is among the techniques used in order to temporarily reduce spasticity, allowing the performance of functional training, such as walking. However, its effects on muscle tone, muscle performance and gait pattern of individuals with chronic hemiparesis have not yet been elucidated. **Objectives:** To investigate the immediate effects of cryotherapy (ice pack) on muscle tone, isometric and isokinetic torque of the dorsiflexor and plantar flexor muscles, and angular and spatiotemporal gait parameters in chronic spastic hemiparetic individuals. **Methods:** *Experimental design:* randomized crossover controlled study. *Participants:* Sixteen chronic hemiparetic subjects. *Intervention:* Cryotherapy (ice pack) or Control Intervention (sand pack at room temperature) applied on the plantar flexor muscles of the paretic limb. *Assessments (pre / post intervention):* 1) Muscle tone, according to the Modified Ashworth Scale (MAS); 2) Spatiotemporal parameters and angular kinematics of the hip, knee and ankle (flexion / extension) during gait obtained through a three-dimensional motion analysis system (Qualisys); 3) Isometric, concentric and eccentric torque of dorsiflexion and flexorplantar, evaluated in isokinetic dynamometer. *Statistical analysis:* Two-way repeated measures ANOVA test was used to analyze all kinematic and torque variables. Non-parametric Wilcoxon and Mann-Whitney tests were used for comparisons of the score in the MAS, since it is considered a categorical variable. Significance level of 0.05 was considered for all statistical analysis. **Results:** Cryotherapy reduced the tone of the plantar flexors, but did not alter the capacity of torque generation or spatiotemporal and angular parameters (sagittal plane) during gait compared to the control intervention. **Conclusion:** The findings of this study suggest that cryotherapy (ice pack) applied on the plantar flexor muscles of individuals with chronic hemiparesis appears to be an effective technique to reduce muscle tone clinically measured but does not affect muscle performance and gait pattern of these individuals.

**Key-words:** Spasticity, Gait, Kinematics, Muscle Strength, Cryotherapy, Stroke.

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**PREFÁCIO**

O projeto que deu origem à presente Tese de Doutorado foi desenvolvido no Laboratório de Pesquisa em Fisioterapia Neurológica (LAFiN), Departamento de Fisioterapia da Universidade Federal de São Carlos. Este estudo dá seguimento à linha de pesquisa que vem sendo desenvolvida no LAFiN sobre a caracterização e reabilitação neurológica de indivíduos com hemiparesia em decorrência de Acidente Vascular Encefálico (AVE).

Esta Tese de Doutorado é composta por dois estudos que têm como objetivo geral avaliar o efeito imediato da crioterapia (pacote de gelo) aplicada sobre a musculatura espástica (neste caso, flexores plantares) de indivíduos com hemiparesia crônica pós-AVE. O primeiro estudo teve como objetivo específico avaliar o efeito desta intervenção sobre o tônus muscular e o padrão de marcha destes indivíduos (Estudo I). Já o segundo estudo investigou o efeito imediato da crioterapia sobre o desempenho muscular de flexores plantares e dorsiflexores (Estudo II). O terceiro estudo oriundo deste projeto está sendo desenvolvido, no qual será avaliado o efeito da crioterapia sobre a resistência passiva destes grupamentos musculares, bem como sua comparação com escalas clínicas de avaliação de tônus.

O Estudo I intitulado "Cryotherapy reduces muscles spasticity, but does not improve post-stroke gait kinematics: a randomized controlled crossover study" foi submetido ao periódico *Physical Therapy Journal* (número de submissão: PTJ-2017-0661). O Estudo II foi intitulado "Cryotherapy does not affect lower limb strength post-stroke: a randomized controlled study" e submetido ao periódico *Journal of Neurologic Physical Therapy* (número de submissão: JNPT-D-17-00197). A análise dos dados do terceiro estudo ainda não foi concluída e, portanto, não será apresentada nesta tese.

Assim, será apresentada nesta tese uma contextualização do trabalho com fundamentação teórica e justificativa para sua realização, bem como os objetivos gerais e hipóteses. Em seguida, serão apresentados os manuscritos oriundos do Estudo I e do Estudo II, nos quais a introdução, os objetivos, os métodos utilizados, os resultados observados, a discussão e a conclusão serão apresentadas para cada estudo, separadamente. Por fim, as atividades desenvolvidas no período do doutorado no âmbito de pesquisa, ensino e extensão serão descritos.

**CONTEXTUALIZAÇÃO**

O Acidente Vascular Encefálico (AVE) tem sido descrito como a terceira causa de morte e principal causa de incapacidade na população adulta mundial (WHO, 2012). Embora cerca de 60% dos indivíduos sobreviventes sejam capazes de deambular após processo de reabilitação (Preston *et al.*, 2011), déficits nas funções dos membros inferiores frequentemente persistem na grande maioria dos casos, afetando a marcha e a mobilidade funcional (Gerrits *et al.*, 2009; Chisholm *et al.*, 2013). A diminuição na velocidade da marcha e um padrão assimétrico são alterações importantes decorrentes do AVE. Entre os fatores que levam a estas alterações no desempenho da marcha destacam-se os déficits observados na articulação do tornozelo (Hsu *et al.*, 2003; Lin *et al.*, 2006).

O controle adequado do tornozelo é de extrema importância para a realização de um padrão normal de marcha (Lin *et al.*, 2006; Di Nardo *et al.*, 2013). Os músculos flexores plantares, como por exemplo, sóleo e gastrocnêmio, atuam essencialmente durante a fase de apoio, controlando excentricamente o avanço do corpo para frente e fornecendo estabilidade ao tornozelo. Ao final da fase de apoio, atuam concentricamente, retirando o calcanhar do solo e assim impulsionando o corpo para frente (Neptune *et al.*, 2001; Di Nardo *et al.*, 2013). Os músculos dorsiflexores, como o tibial anterior, são ativados em toda a fase de balanço, permitindo o avanço do pé sem que este se choque contra o solo. Eles posicionam adequadamente o tornozelo em dorsiflexão para possibilitar o apoio inicial do calcanhar na fase de apoio seguinte (Di Nardo *et al.*, 2013).

Em indivíduos hemiparéticos, os movimentos do tornozelo encontram-se alterados. Dentre as alterações decorrentes do AVE, está a fraqueza muscular, reconhecida clinicamente como um dos principais fatores limitantes da funcionalidade durante a fase crônica (Neckel *et al.*, 2006). Diversos fatores podem levar a esta diminuição de força gerada pelos flexores plantares e dorsiflexores do tornozelo no membro parético, incluindo componentes neurais e musculares. A falha na ativação voluntária dos flexores plantares (Klein *et al.*, 2010) e dorsiflexores (Chou *et al.*, 2013) parece ser um dos principais fatores causais da fraqueza observada. Além da menor ativação muscular, desordens temporais acompanham os músculos paréticos (Marigold *et al.*, 2004). A coativação da musculatura antagonista também parece ser um fator contribuinte para a fraqueza da musculatura do tornozelo (Chow *et al.*, 2012), embora os resultados de estudos recentes suportem a ideia de que a atividade antagonista não seja a causa primária da fraqueza observada em indivíduos hemiparéticos crônicos (Klein *et al.*, 2010).

Outro aspecto importante refere-se às modificações intrínsecas do músculo esquelético em decorrência das alterações do sistema nervoso central pós-AVC. O aumento da resistência passiva observada principalmente nos flexores plantares pode dificultar a dorsiflexão durante a marcha (Lamontagne et al., 2002; Gao et al., 2009). Este aumento da resistência passiva pode ocorrer devido a uma deposição de tecido não contrátil nesta musculatura, em especial tecido conjuntivo e gorduroso (Ramsay et al., 2011; Zhang et al., 2013), bem como alterações no tecido contrátil, dentre elas a atrofia muscular (Ramsay et al., 2011), redução do número de sarcômeros ao longo da fibra e/ou redução no comprimento do sarcômero. Assim, estas alterações podem contribuir diretamente para o déficit de amplitude de movimento (ADM), aumento da resistência passiva e fraqueza muscular observados no tornozelo do membro parético pós-AVC (Gao et al., 2009; Zhang et al., 2013).

Não menos importante, a espasticidade também é uma alteração frequentemente observada em decorrência do AVE (Li *et al.*, 2017). A espasticidade pode ser conceituada como uma desordem motora caracterizada pelo aumento velocidade-dependente nos reflexos tônicos frente ao alongamento (Lance, 1980; Sommerfeld *et al.*, 2004), embora o aumento da resistência ao alongamento possa ocorrer devido não apenas a hiperatividade reflexa, mas também a alterações intrínsecas do tecido muscular (Sinkjaer *et al.*, 1993; Chung *et al.*, 2008). Embora sua contribuição para déficits de marcha seja controversa na literatura (Ada *et al.*, 1998; Hsu *et al.*, 2003; Lin *et al.*, 2006; Chisholm *et al.*, 2013), alguns estudos evidenciam a relação da espasticidade com o déficit no desempenho de tarefas funcionais, como a marcha, pós-AVE (Hsu *et al.*, 2003; Lin *et al.*, 2006). É descrita como a principal causa de assimetria espacial durante a marcha, já que a espasticidade dos flexores plantares, elicitada pelo alongamento desta musculatura no membro parético na fase de apoio, dificulta o avanço do centro de gravidade para frente, resultando em menor comprimento do passo do outro membro (Lin *et al.*, 2006). Além disso, a espasticidade deste grupamento muscular foi descrita como um fator determinante para a assimetria temporal da marcha, ou seja, a espasticidade dos flexores plantares leva os indivíduos a realizarem movimentos compensatórios com o quadril e joelho para conseguir dar o passo. Desta forma, a fase de balanço do membro parético apresenta uma trajetória alterada, com maior duração (Hsu *et al.*, 2003).

Neste âmbito, diversas intervenções são aplicadas na prática clínica com o intuito de minimizar temporariamente a espasticidade, a fim de possibilitar o treino funcional sem, ou com reduzida, influência deste fator. A crioterapia está entre as técnicas mais utilizadas. No entanto, há uma carência de estudos que avaliem o real efeito da aplicação de gelo nos diferentes aspectos que podem sofrer influência da mesma. A crioterapia é definida como a aplicação de qualquer substância que retira calor do corpo, resultando em diminuição da temperatura tecidual (Nadler *et al.*, 2004). Em indivíduos saudáveis, os efeitos fisiológicos da crioterapia incluem a redução no fluxo sanguíneo e diminuição do metabolismo local, bem como redução na velocidade de condução nervosa sensorial e motora (Algafly e George, 2007; Herrera *et al.*, 2011). No entanto, estudos que avaliaram o efeito da crioterapia sobre o desempenho muscular são controversos.

Um recente estudo (Vieira *et al.*, 2013) avaliou o desempenho isométrico e concêntrico dos flexores plantares após aplicação de diferentes tipos de crioterapia, por 20 min, como a aplicação de pacote de gelo na região posterior da perna e imersão da perna em água gelada, em indivíduos saudáveis. Foi observado um aumento no pico de torque isométrico após aplicação de pacote de gelo. Além disso, tanto o pacote de gelo como a imersão em água gelada diminuíram o pico de torque e trabalho total durante contração concêntrica (Vieira *et al.*, 2013). Por outro lado, um estudo realizado anteriormente, também com indivíduos saudáveis (Hatzel e Kaminski, 2000), com imersão da perna em água gelada, não observou mudanças no pico de torque concêntrico ou excêntrico durante a flexão plantar, inversão ou eversão do tornozelo. Uma redução no pico de torque concêntrico foi observada apenas durante a dorsiflexão. Do mesmo modo Kimura e colaboradores (1997) não observaram mudanças no pico de torque excêntrico na flexão plantar após imersão, embora tenha ocorrido um aumento no trabalho total após intervenção. Ainda, Hopkins e colaboradores (2002) observaram um aumento no pico de torque concêntrico dos flexores plantares logo após aplicação de pacote com gelo, sendo que este padrão foi mantido por 60 minutos após aplicação. Tais disparidades podem ser explicadas pelas diferenças nas técnicas de resfriamento tecidual (Hopkins e Stencil, 2002; Vieira *et al.*, 2013) e evidenciam a falta de consenso na literatura sobre os efeitos da crioterapia mesmo em indivíduos saudáveis.

Em indivíduos hemiparéticos crônicos, são escassos os estudos que avaliam o efeito da crioterapia. Além disso, ainda não há consenso em relação a sua efetividade nesta população. Price et al. (1993) avaliaram o efeito da aplicação de crioterapia em indivíduos com espasticidade secundária a traumatismo crânio-encefálico, lesão medular e AVE. Baseando-se em medidas de resistência viscoelástica dos flexores plantares de tornozelo, foi observada uma redução nos níveis de espasticidade após 20 minutos de aplicação de pacote de gelo, embora 2 dos 25 sujeitos tenham apresentado resultados contrários. Por outro lado, um estudo recente (Martins *et al.*, 2012) avaliou o efeito imediato da crioterapia (pacote de gelo) sobre a excitabilidade reflexa e atividade muscular voluntária em indivíduos hemiparéticos crônicos. Embora tenham sido observadas alterações favoráveis à diminuição da espasticidade, como o aumento da latência do reflexo-H, a amplitude pico do reflexo-H também se apresentou elevada, sendo que nenhuma destas alterações foi suficiente para modificar o padrão de ativação do tibial anterior após aplicação de crioterapia.

Desta forma, mais estudos de caracterização dos mecanismos de resposta neuromuscular frente à aplicação de gelo ainda são necessários para o embasamento científico desta prática dentro do programa de reabilitação de indivíduos hemiparéticos crônicos. A efetividade da crioterapia precisa ser considerada de forma abrangente, isto é, devem ser observadas não apenas variáveis que podem ser diretamente influenciadas pela aplicação de gelo, mas também o quanto estas alterações refletem na funcionalidade do indivíduo. Portanto, o presente estudo teve como objetivo investigar os efeitos imediatos da crioterapia (pacote de gelo) sobre o tônus muscular, o torque isométrico e isocinético em flexão plantar e dorsiflexão, e os parâmetros angulares e espaço-temporais da marcha em indivíduos hemiparéticos espásticos crônicos. A hipótese inicial deste estudo é que a aplicação de crioterapia seria capaz de reduzir temporariamente a espasticidade, apresentando efeitos limitados na geração de força e padrão de marcha dos indivíduos com hemiparesia espástica crônica.

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# ESTUDO I

# Cryotherapy reduces muscles spasticity, but does not improve post-stroke gait kinematics: a randomized controlled crossover study

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## Abstract

*Background:* Lower limb impairments often persist following stroke, affecting gait and functional mobility. In this context, several interventions are used in clinical practice to optimize functional performance. Following the premise that spasticity might affect gait post-stroke, cryotherapy is among the techniques still used in some clinical rehabilitation centers to reduce spasticity temporarily, aiming at facilitating the performance of functional training, such as walking. However, the understanding of whether a decrease in spasticity level, if any, would lead to an improvement in gait parameters is not evidence-based and needs to be elucidated. *Objective:* to investigate the immediate effects of cryotherapy (ice pack modality), applied to spastic plantarflexor muscles of subjects post-stroke, on spasticity level and angular/spatiotemporal gait parameters. *Design:* This is a randomized controlled crossover study. *Setting: Patients:* Sixteen chronic hemiparetic subjects participated in this study. *Intervention:* Cryotherapy (ice pack) or Control Intervention (room temperature sand pack) applied on the calf muscles of the paretic limb. *Measurements:* 1) Tonus according to the Modified Ashworth Scale; and 2) Spatiotemporal and angular kinematics of the hip, knee and ankle (flexion/extension), obtained using a tridimensional movement analysis system (Qualisys), before and immediately after intervention. *Results:* Cryotherapy decreased plantarflexor tonus but did not affect spatiotemporal parameters or ankle, knee and hip flexion/extension during gait, compared to control application. *Limitations:* The results of this study are limited to the immediate effects of ice pack modality cryotherapy on spasticity and gait parameters in subjects with chronic hemiparesis post-stroke with mild or moderate spasticity. *Conclusions:* Cryotherapy (ice pack) applied on the calf muscles of the paretic limb in chronic hemiparetic subjects reduces muscle spasticity, but does not improve gait parameters.


**Key-words:** Muscle Tonus, Walking, Cryotherapy, Cerebrovascular Disease

**Introduction**

Stroke is one of the leading causes of disability in adults worldwide.[1, 2] Hemiparesis following stroke is associated with significant lower limb impairment, functional mobility limitation, and reduced social participation.[3] Although about 60% of stroke survivors are able to walk after rehabilitation,[4] deficits in lower limb functions and gait frequently persist in the vast majority of cases.[4-6] Ankle-related impairments are among the contributing factors that lead to changes in gait performance.[7-10] Muscle weakness,[8, 10] poor motor control, such as abnormal muscle activation and deficits in synergies,[7, 9, 11-13] and passive stiffness of the plantarflexors,[14, 15] are among the factors that contribute to changes in gait post-stroke. Spasticity is another common impairment observed post-stroke,[16, 17] although its contribution for gait deficits are controversial in the literature.[5, 8, 18, 19]

Some previous studies have shown that it is unlikely that spasticity negatively influences gait post-stroke.[18, 20] For example, spastic stroke patients did not exhibit an increase in resistance to dorsiflexion during gait, specifically during the single support phase, compared to control subjects.[18] Another study that aimed at identifying the most important clinical variables determining gait speed in persons with stroke showed other factors such as plantarflexor strength, but not spasticity, as important factors to consider in determining the gait capacity of chronic stroke subjects.[20]

On the other hand, some studies have shown a relationship between spasticity and gait asymmetry.[8, 19] Spasticity of the plantarflexor muscles has been related to spatial asymmetry during gait, following the premise that the spasticity makes it difficult to advance the center of gravity forward during the paretic limb support phase, resulting in a decrease in non-paretic limb step length.[19] In addition, the spasticity was described as a determinant factor for the temporal asymmetry of gait. That is, the spasticity of the plantar flexors would lead the individual to compensatory movements with the hip and knee, altering the trajectory of the paretic limb during the swing phase, which would present a longer duration.[8]

Despite these controversial findings, several interventions are still used in clinical practice in order to temporarily minimize spasticity[21-23] and there is a considerable focus on the effects of spasticity on gait after stroke.[8, 19] Specifically, in the case of the immediate effects of cryotherapy on spasticity, the rationale used by clinicians for the application of this treatment is that it will temporarily reduce spasticity so that a more normal gait pattern can be practiced. However, to the best of our knowledge, there is no evidence reporting if the temporary decrease in spasticity following cryotherapy, if any, would have a positive effect on gait parameters in those with chronic hemiparesis after stroke.

Thus, the aim of this study was to investigate the immediate effects of cryotherapy (ice pack modality), applied to spastic plantarflexor muscles of subjects post-stroke, on spasticity level and on gait parameters in those with spastic chronic hemiparesis post-stroke. Gait parameters evaluated include 1) spatiotemporal variables, such as gait speed, and 2) ankle, knee and hip angles in the sagittal plane at initial contact and swing phase during gait. We hypothesized that cryotherapy would decrease spasticity level and would result in limited improvement of gait performance. The results of this study will provide importance evidence for the immediate effects of the reduction of spasticity on gait after stroke that will assist clinicians in their evidence based approach to the use of such techniques.

**Methods**

*Experimental Design Overview*

This study was a single-blind, randomized controlled crossover trial, conducted with persons with chronic hemiparesis after stroke at a single center (Federal University of São Carlos - UFSCar, Brazil). Subjects were recruited from a variety of sources including the UFSCar rehabilitation center (São Carlos, SP, Brazil), the University Hospital of São Carlos

(São Carlos, SP, Brazil) and through advertisements. The Ethics Committee in Brazil approved the protocol (Number: 1.469.151) and the study was registered in the Clinical Trials (URL: http://www.clinicaltrials.gov. Unique identifier: NCT02736747). All participants provided written informed consent.

Assessments were divided into five days. On the first day (Day 0), a screening assessment was performed to select the sample according to inclusion and exclusion criteria. On the same day, a clinical assessment was performed if the participant met the criteria. Then, enrolled subjects were assessed in two evaluation blocks, consisting of two evaluation/intervention days each (Day 1 and Day 2). On Day 1, the level of spasticity of the plantar flexors and dorsiflexors was assessed and scored according to the Modified Ashworth Scale, before and immediately after the intervention (Control or Cryotherapy). On Day 2, gait kinematic assessment was performed, also pre- and post-application of intervention (Control or Cryotherapy). Seven days rest period between each assessment and a wash-out period of fifteen days between blocks were completed. In each block, one of two interventions (Control or Cryotherapy) was applied in both days (Day 1 and Day 2) and switched to the other intervention in the second block. Enrolled subjects were randomly assigned to one of two groups to receive Control Intervention first or Cryotherapy Intervention first. Sealed opaque envelopes prepared by an independent member of staff were used for randomization implementation. The assessments were performed on separate days to avoid testing at a time when limb temperature would have returned to baseline levels. A schematic representation of the study experimental design is shown in Figure 1.

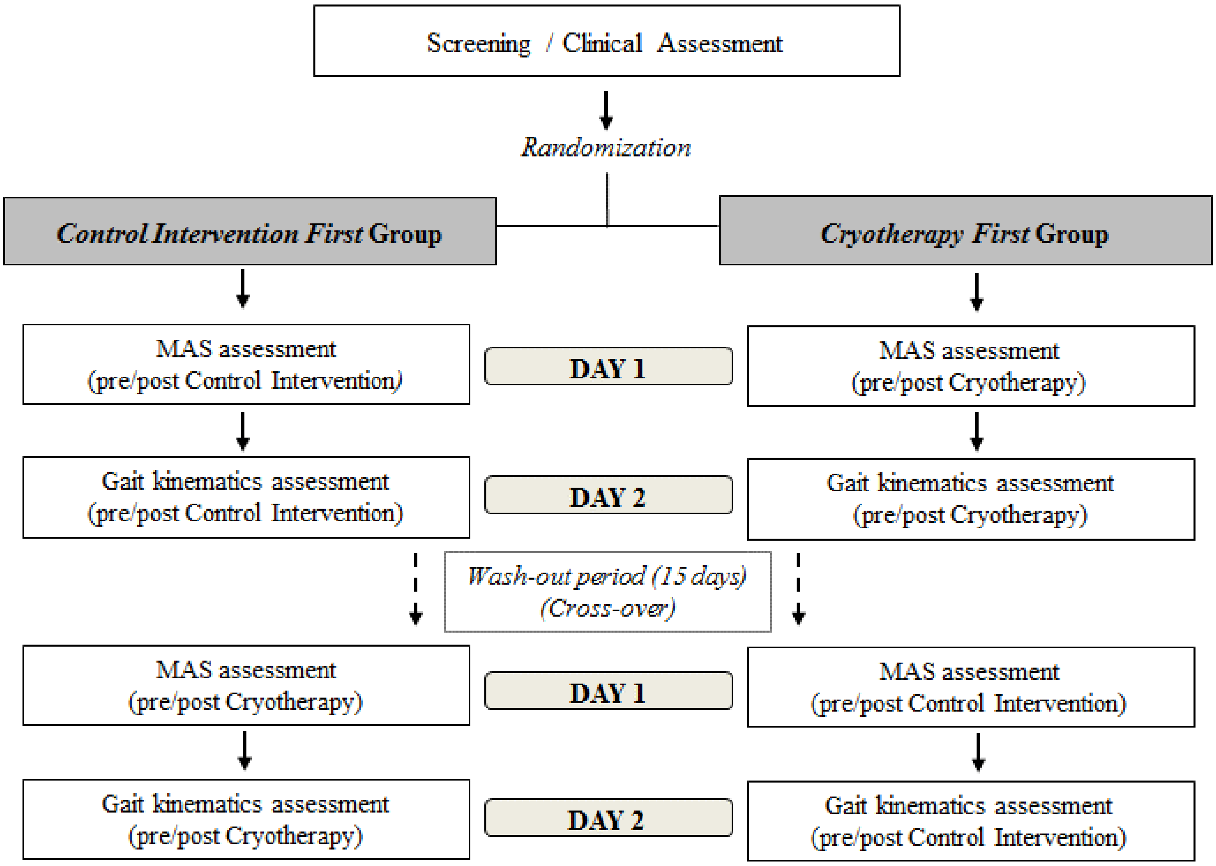


**Figure 1.** Experimental design of the study. Abbreviations: MAS, Modified Ashworth Scale.

*Participants*

The following inclusion criteria were considered: (1) chronic hemiparesis (post-stroke time greater than 6 months) due to unilateral ischemic stroke of either hemisphere; (2) age between 40 and 75 years; (3) spasticity levels between 1 and 3 according to MAS[24] of the ankle flexor muscles; (4) walking ability classified as level 3, 4 or 5 according to the Functional Ambulation Category (FAC)[25]; (5) minimum score on the Mini-Mental State Examination, according to the subject's educational level [26, 27].

The following exclusion criteria were considered: (1) peripheral neuropathy; (2) intolerance to the ice pack application; (3) presence of Raynaud's phenomenon; (4) ulcers or skin lesions in the location of the intervention application; (5) serious cardiovascular or peripheral vascular disease (heart failure, arrhythmia or angina pectoris); (6) any other orthopedic or neurological disorder; botulinum toxin application up to six months before the study; (7) lower limbs joint or previous muscle injuries; (8) pain during the assessment/intervention procedures.

*Clinical assessment*

In order to characterize the subjects enrolled in this study, a clinical evaluation was carried out, which included 1) collection of personal data, such as age and stroke related information; 2) collection of anthropometric data, such as weight and height; 3) evaluation of lower-limb sensorimotor impairment according to the Fugl Meyer Scale [28]; 4) passive range of motion (ROM) for dorsiflexion and plantar flexion using a goniometer (the goniometry was performed with the patient sitting on a stretcher, with their leg suspended and knee in a neutral position at 90° flexion).

*Spasticity assessment*

The resistance to passive movement for ankle plantarflexor muscles was evaluated before and after intervention (control/cryotherapy) and scored according to the Modified Ashworth Scale (MAS)[24]. This scale was used considering that an increase in muscle tonus is one of the main components of spasticity post-stroke, and therefore, it has been used in several studies as a spasticity parameter pre and/or post intervention.[29-31] Subjects lay on their side on a mat table and the evaluator performed a fast dorsiflexion movement from a maximum plantar flexion. The MAS consists of six levels of spasticity, which range from 0, characterized as "normal tonus" or "no increase in muscle tone" to 4, "stiffness of affected part" or "limited range of motion". For statistical purposes, the MAS score (0, 1, 1+, 2, 3, 4) was considered as 0, 1, 2, 3, 4, and 5, respectively.

*Gait kinematics assessment*

A motion capture system analysis (Qualisys, Qualisys Inc., Gothenburg, Sweden) consisting of seven cameras was used to analyze spatiotemporal and tridimensional angular kinematics of the hip, knee and ankle before and after the cryotherapy/control intervention. Reflexive passive markers were positioned on the following anatomical references: bilaterally on the first, second and fifth metatarsal heads, medial and lateral malleoli, medial and lateral epicondyle of the femur, major trochanters, iliac crests, acromion, C7 and sternum. Clusters of rigid reflective markers were positioned at T4, T10, bilaterally on the lateral faces of the thighs and legs. All kinematic data were collected with a sampling frequency of 120 Hz. Participants were instructed to walk barefoot, at a self-selected and comfortable speed along the 10-meter walkway.[32]

All kinematic data were filtered with a fourth-order zero-lag filter, Butterworth low pass at 6 Hz. Visual 3D ™ software (C-Motion, Inc., Rockville, MD, USA) was used to calculate spatiotemporal and angular kinematics. The joint kinematics was calculated using the joint coordinate system recommended by the International Society of Biomechanics[33, 34] and was expressed relative to the static anatomical position. For each gait cycle, the following angular kinematic variables of the paretic limb were calculated: ankle, knee and hip angles in the sagittal plane at initial contact and at toe-off, and peak angle for ankle, knee and hip in the sagittal plane during swing phase.[35] The spatiotemporal parameters were: swing and stance time, stride length, gait velocity, cadence.[36] For data analysis, data of the first 2-3 trials of gait assessment (i.e., 2-3 strides) were considered to calculate the outcome variables before and after the cryotherapy/control application. Kinematic data were processed using Matlab software (The MathWorks, Natick, Massachusetts).

*Interventions*

All assessments were performed by the same experienced physiotherapist, who was blinded to intervention used, whereas the intervention applications were performed by another research team member. Participants were instructed to avoid intake of stimulants such as alcohol, caffeine and chocolate 2 hours before the intervention and to not exercise for at least 4 hours beforehand.[37] All procedures were performed from 2pm to 6pm in order to minimize the possible effects of the circadian rhythm. The room temperature was controlled at 25ºC in all procedures, and subjects rested for a period of 15 minutes in the evaluation room for acclimatization at the beginning of the assessment/intervention sessions.[38]

A rectangular area was defined to delimitate where the pack was placed as described by Herrera.[37] For the cryotherapy intervention, the pack (25 x 35cm) was filled with 1000g of crushed ice tied around the leg using a non-compressive elastic band. For the control intervention, the pack was filled with 1000 g of sand, at room temperature. The comparison between cryotherapy and control intervention was delineated in order to clarify the effect of cooling *versus* other effects that could interfere with the dependent variables assessed in this study.

The participants were positioned in a comfortable chair for the intervention application. The leg was covered by a strap of plastic film, avoiding direct contact between the skin and the pack. Then, the pack (cryotherapy - ice; control - sand) was placed over the delimited area and maintained for 20 minutes. The subjects remained with the limb resting and neither ice nor sand was added during the application time.

*Data Analysis*

The non-parametric Wilcoxon test was performed to compare the spasticity level (MAS score) pre and post-intervention (cryotherapy and control), since it is considered a categorical variable. In addition, for comparisons between groups in each evaluation the Mann-Whitney test was used. For all angular and spatiotemporal parameters, a mixed two-way ANOVA with repeated measures with Bonferroni correction was used to verify the effect of interaction (group and evaluation time), evaluation time (before and after cryotherapy and control interventions) and group (cryotherapy first and control first). Partial $\eta^2$ is presented and a value of 0.2, 0.5, and 0.8 corresponds to a small, medium, and large effect, respectively[39]. A significance level of 0.05 was considered and all statistical tests were performed using SPSS software, version 17.0 (SPSS Inc., Chicago, IL, USA).

## Results

### *Participants*

Four hundred and twenty nine persons with hemiparesis following stroke from the local community in São Carlos, SP (Brazil) were assessed for eligibility. From these subjects, 16 met the criteria and were enrolled in the study. They were randomly allocated to Control First Group (PL, n=9) or Cryotherapy First Group (CT, n=7). All participants completed the experimental procedures and the data analysis was successfully conducted for all 16 participants (Figure 2). No adverse effects were observed during data collection.

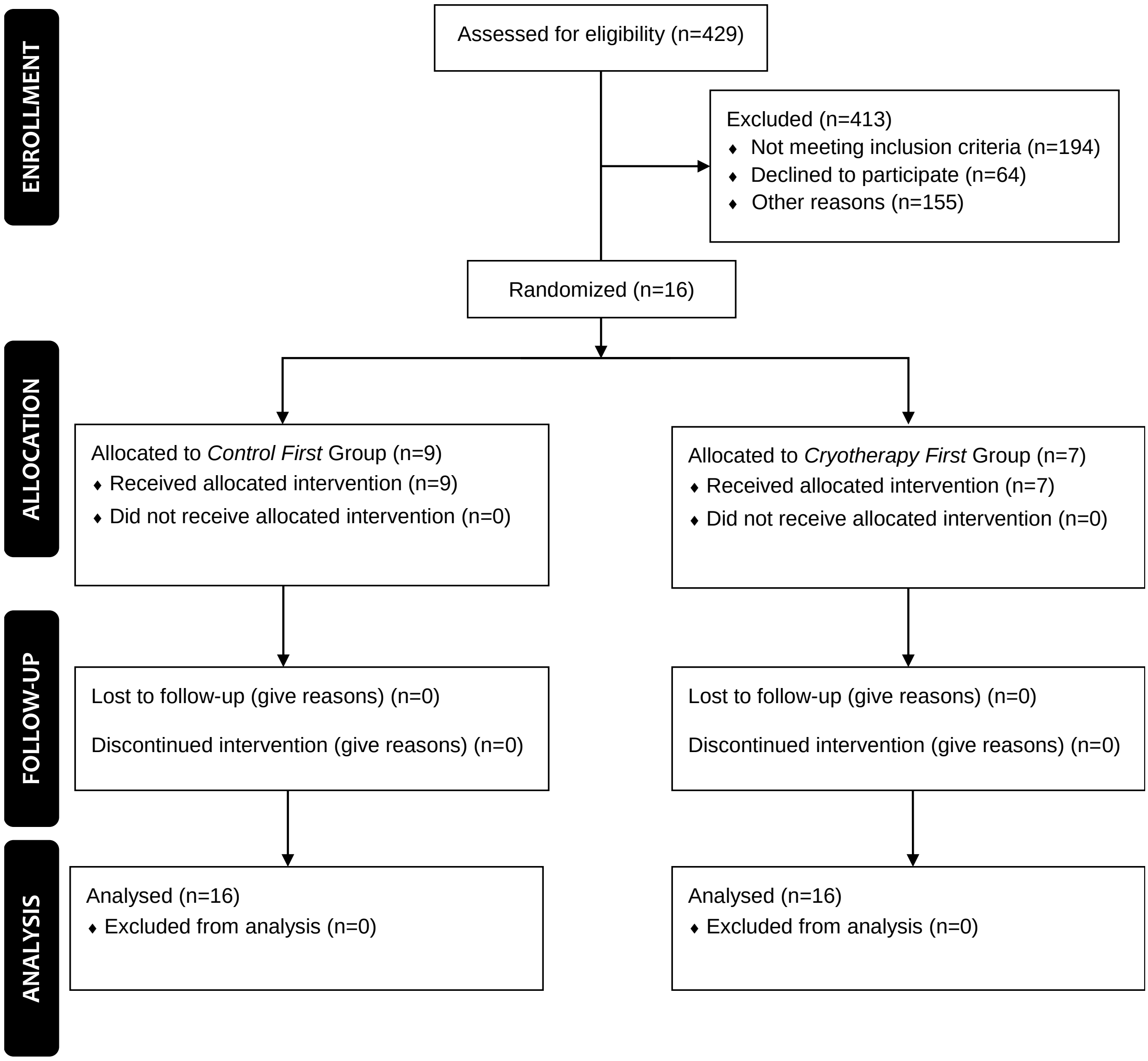


**Figure 2.** Flow diagram of study.

Characteristics of the participants are presented in Table 1. The mean age was 62 (min: 52 – max: 71) years old. Six participants had right hemisphere stroke and the average time post-stroke was 29 months. In relation to plantarflexor muscle tone during baseline, ten participants presented a score of 1+, five individuals a score of 2 and 1 individual a score of 3 on the MAS. The average comfortable walking speed was 0.77 m/s.

**Table 1.** Sample characterization

| *Outcomes* | *Values* |
|---|---|
| Age (years) | 62.3 (52-71) |
| BMI (Kg/m2) | 24.81 (21.36-31.89) |
| Gender (F/M) | 2/14 |
| Dominant side (R/ L) | 15/0 |
| Hemiparesis Side (R/L) | 9/6 |
| Time post-stroke (months) | 29 (20-135) |
| Passive ROM of ankle dorsiflexion (º) | 12.5 (5-32) |
| Passive ROM of ankle plantarflexion (º) | 42.1 (32-52) |
| MAS of ankle plantar flexors muscles (0/1/1+/2/3/4) | (0/0/10/5/1/0) |
| FMA-LE, total score | 81 (65-98) |
| FMA-LE, subscale score of sensibility | 11 (4-12) |
| FMA-LE, subscale score of motor function | 21 (13-34) |
| Comfortable Walking Speed (m/s) | 0.77 (±0.24) |

Abbreviations: BMI, Body Mass Index; F, Female; M, Male; R, Right; L, Left; ROM, Range of Motion; FMA-LE, Fugl-Meyer Assessment - Lower Extremity; MAS, Modified Ashworth Scale. Data expressed as mean (minimum-maximum), except FMA-LE, expressed as median (minimum-maximum), Comfortable Walking Speed as mean (standard deviation) and MAS, expressed as number of subjects in each category/score.

*Cryotherapy effect on spasticity*

Cryotherapy application (ice pack) decreased plantar flexor muscle tone according to MAS score (p=0.002, effect size=0.8). No difference was observed between pre and post control intervention on MAS score (p=0.157). Regarding intergroup comparisons, no differences were observed between the groups at baseline (p=0.456), whereas plantarflexor muscle tone presented lower levels post cryotherapy compared to post control (p<0.001). Figure 3 shows MAS score results for all groups and assessments.

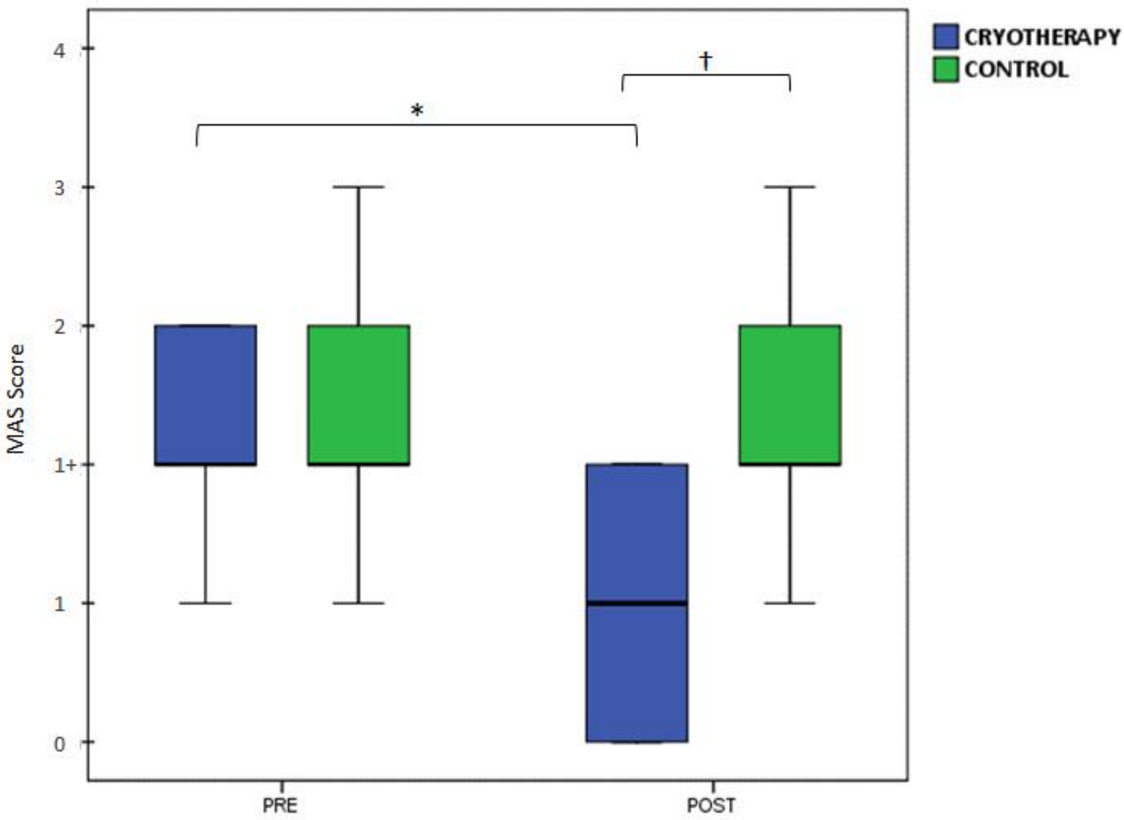


**Figure 3.** Tonus outcome according to Modified Ashworth Scale. *Significant difference between pre and post assessment. † Significant difference between Cryotherapy and Control group. Abbreviations: MAS, Modified Ashworth Scale.

*Cryotherapy effect on gait*

Overall, cryotherapy did not influence gait angular kinematics or spatiotemporal parameters. In order to better understand the cryotherapy effect on gait angular kinematics, the sagittal ankle, knee and hip kinematic waveforms during gait for the paretic limb were plotted (Figure 4). The mean curve and standard deviation across all subjects were plotted time-normalized by the gait cycle (100%), pre and post cryotherapy intervention. Qualitatively, no changes in the waveforms are observed after cryotherapy application.

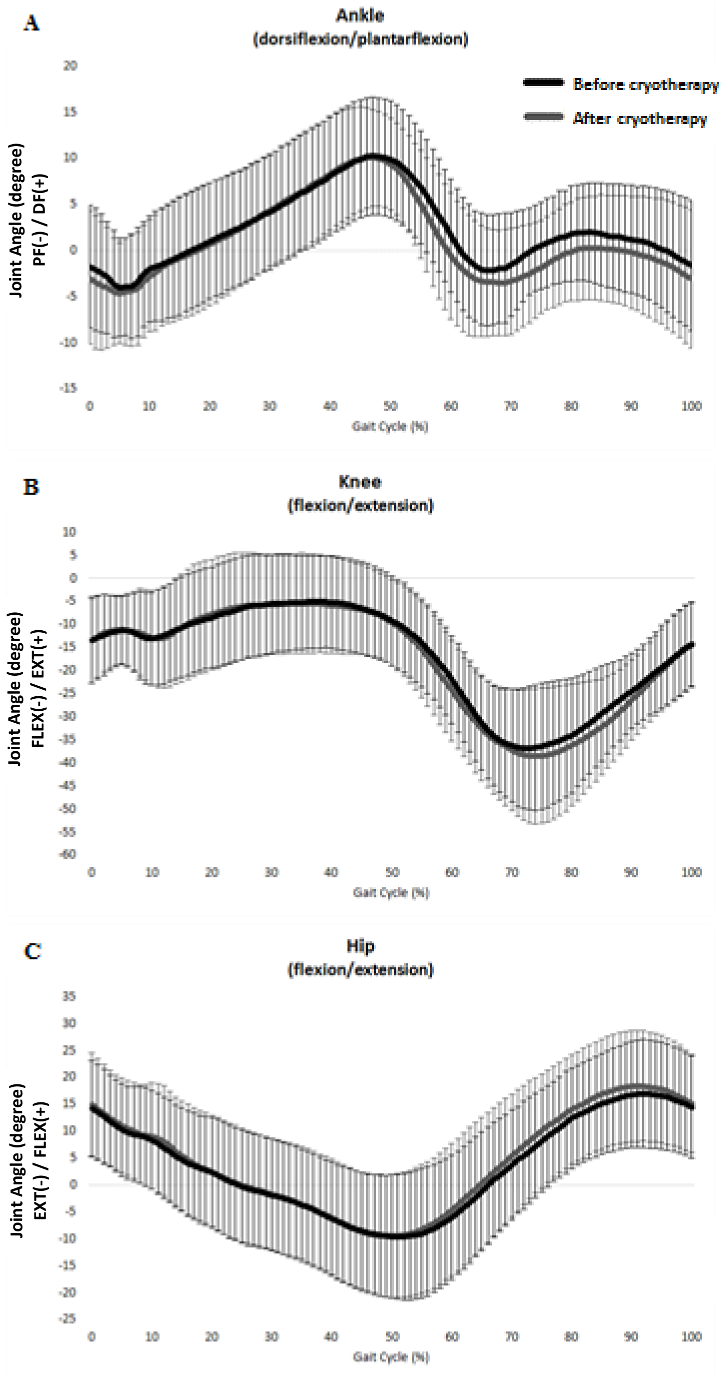


**Figure 4.** Paretic limb kinematics waveforms during gait before and after cryotherapy application. Ankle plantarflexion/dorsiflexion (A), knee flexion/extension (B) and hip flexion/extension (C) mean curve and standard deviation across all subjects are plotted time-normalized by the gait cycle (100%). Abbreviations: PF, Plantarflexion; DF, Dorsiflexion; EXT, Extension; FLEX, Flexion.

There was no significant interaction between the group (cryotherapy first / control first) and evaluation time (pre / post intervention) for any of the angular kinematic and spatiotemporal parameters assessed. Furthermore, there was no group effect on any angular and spatiotemporal outcomes ($p>0.05$), demonstrating that the order of intervention (cryotherapy first or control first) did not influence the results. No differences were observed between pre-intervention in the first block of evaluation/treatment and pre-intervention in the second block ($p>0.05$), regardless of the group (cryotherapy first or control first), confirming that the baseline measurements were similar. An overview of the results of mixed two-way ANOVA for angular and spatiotemporal parameters are presented in the supplementary material (Table S1).

**Table 1S**. Overview of the results of mixed two-way ANOVA for angular and spatiotemporal parameters.

| | | Effect of Evaluation | | | | Effect of Evaluation X Group | | | | Effect of Group | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Parameter** | **Measure** | df | F | P value | Partial $\eta^2$ | df | F | P value | Partial $\eta^2$ | df | F | P value | Partial $\eta^2$ |
| Angular | Ankle dorsiflexion/ plantarflexion (initial contact) | 3 | 6.399 | 0.001* | 0.314 | 3 | 2.714 | 0.057 | 0.162 | 1 | 0.101 | 0.755 | 0.007 |
| | Knee flexion/extension angle (initial contact) | 1.65 | 1.610 | 0.222 | 0.103 | 1.65 | 1.092 | 0.341 | 0.072 | 1 | 1.237 | 0.285 | 0.081 |
| | Hip flexion/extension angle (initial contact) | 1.61 | 0.876 | 0.409 | 0.059 | 1.61 | 0.462 | 0.595 | 0.032 | 1 | 0.087 | 0.773 | 0.006 |
| | Ankle dorsiflexion/plantarflexion (toe-off) | 3 | 8.203 | 0.000* | 0.369 | 3 | 0.313 | 0.816 | 0.022 | 1 | 0.627 | 0.442 | 0.043 |
| | Knee flexion/extension (toe-off) | 1.44 | 2.524 | 0.118 | 0.153 | 1.44 | 0.226 | 0.727 | 0.016 | 1 | 1.715 | 0.211 | 0.109 |
| | Hip flexion/extension (toe-off) | 1.55 | 1.620 | 0.222 | 0.104 | 1.55 | 1.183 | 0.314 | 0.078 | 1 | 0.511 | 0.486 | 0.035 |
| | Peak ankle dorsiflexion (swing phase) | 1.81 | 7.323 | 0.004* | 0.343 | 1.81 | 0.987 | 0.379 | 0.066 | 1 | 0.365 | 0.555 | 0.025 |
| | Peak knee flexion (swing phase) | 1.54 | 2.016 | 0.164 | 0.126 | 1.54 | 0.353 | 0.652 | 0.025 | 1 | 1.863 | 0.194 | 0.117 |
| | Peak hip flexion (swing phase) | 1.79 | 3.582 | 0.047* | 0.204 | 1.79 | 0.524 | 0.579 | 0.036 | 1 | 0.023 | 0.883 | 0.002 |
| Spatiotemporal | Stance time | 1.69 | 4.614 | 0.025* | 0.248 | 1.69 | 0.290 | 0.715 | 0.020 | 1 | 1.108 | 0.310 | 0.073 |
| | Swing time | 3 | 5.252 | 0.004* | 0.273 | 3 | 0.618 | 0.607 | 0.042 | 1 | 1.336 | 0.267 | 0.087 |
| | Stride length | 1.69 | 2.205 | 0.139 | 0.136 | 1.69 | 3.522 | 0.053 | 0.201 | 1 | 2.511 | 0.135 | 0.152 |
| | Gait velocity | 1.72 | 5.349 | 0.015* | 0.276 | 1.72 | 2.670 | 0.096 | 0.160 | 1 | 3.672 | 0.076 | 0.208 |
| | Cadence | 1.32 | 3.090 | 0.086 | 0.181 | 1.32 | 0.829 | 0.407 | 0.056 | 1 | 1.512 | 0.239 | 0.097 |

The main effect of evaluation time (pre/post cryotherapy or control intervention) showed that there was no difference among evaluation time points in knee flexion/extension angle at initial contact (F=1.610, p=0.222), hip flexion/extension angle at initial contact (F=0.876, p=0.409), knee flexion/extension angle at toe-off (F=2.524, p=0.118), hip flexion/extension angle at toe-off (F=1.620, p=0.222), peak knee flexion angle during swing phase (F=0.383, p=0.634), stride length (F=2.205, p=0.139) and cadence (F=3.090, p=0.086). However, there was an effect of the evaluation time (pre- and post- cryotherapy or control intervention), regardless of the intervention used (cryotherapy or control), in ankle dorsiflexion/ plantarflexion angle at initial contact (F=6.399, p=0.001, partial $\eta^2$=0.314), ankle dorsiflexion/plantarflexion angle at toe-off (F=8.203, p<0.001, partial $\eta^2$=0.369), peak ankle dorsiflexion angle during swing phase (F=7.323, p=0.004, partial $\eta^2$=0.343), peak hip flexion angle during swing phase (F=3.582, p=0.047, partial $\eta^2$=0.204), stance time (F=4.614, p=0.025, partial $\eta^2$=0.248), swing time (F=5.252, p=0.004, partial $\eta^2$=0.273), gait velocity (F=5.349, p=0.015, partial $\eta^2$=0.276).

Pairwise comparisons showed discrete changes post treatment, regardless of the intervention applied (cryotherapy or control). A decrease in ankle dorsiflexion at initial contact post-intervention in the second block of evaluation (p=0.023), an increase in ankle plantarflexion at toe-off post-intervention in the first block of evaluation (p=0.001), a decrease in ankle dorsiflexion during swing phase post-intervention at the first (p=0.002) and second blocks (p=0.047), an increase in gait speed post-intervention at the first (p=0.005) and second blocks (p=0.029) were observed. Table 2 presents gait angular and spatiotemporal parameters results (mean and standard deviation) for all evaluation times (pre/post cryotherapy or control).

**Table 2.** Angular kinematic (sagittal plane) and spatiotemporal parameters during gait for paretic limb (ankle, knee and hip), pre and post interventions (control or cryotherapy).

| *Parameter* | *Measure* | *Group* | *Intervention* | | | |
|---|---|---|---|---|---|---|
| | | | *Cryotherapy* | | *Control* | |
| | | | Pre | Post | Pre | Post |
| **Angular** | **Heelstrike** (º) | | | | | |
| | Ankle * DF(+)/PF(-) | Cryotherapy first | -1.45 (5.67) | -3.00 (5.95) | -1.42 (5.35) | -3.75 (5.62)* |
| | | Control first | -1.93 (7.61) | -2.95 (8.42)* | -0.19 (7.70) | -0.15 (7.75) |
| | Knee * EXT(+)/FLEX(-) | Cryotherapy first | -16.02 (7.80) | -17.59 (8.71) | -17.11 (6.35) | -16.70 (7.12) |
| | | Control first | -11.55 (10.03) | -10.02 (9.12) | -12.84 (9.65) | -14.01 (10.35) |
| | Hip * FLEX(+)/EXT(-) | Cryotherapy first | 14.95 (10.20) | 17.31 (11.16) | 14.41 (6.43) | 15.29 (6.04) |
| | | Control first | 13.61 (8.40) | 12.99 (8.53) | 15.42 (10.12) | 14.79 (11.82) |
| | **Toe-off** (º) | | | | | |
| | Ankle * DF(+)/PF(-) | Cryotherapy first | -2.83 (6.70) | -5.35 (8.06)* | -5.33 (7.41) | -6.52 (7.44) |
| | | Control first | -2.29 (5.58) | -3.73 (5.44) | -0.99 (6.45) | -2.67 (6.68)* |
| | Knee * EXT(+)/FLEX(-) | Cryotherapy first | -30.28 (10.12) | -32.19 (9.83) | -31.08 (8.67) | -33.64 (9.36)* |
| | | Control first | -37.06 (7.23) | -38.33 (7.95)* | -36.48 (8.70) | -37.58 (8.72) |
| | Hip * FLEX(+)/EXT(-) | Cryotherapy first | 1.45 (10.22) | 2.70 (10.53) | -1.28 (8.88) | 1.33 (7.41) |
| | | Control first | -2.70 (10.22) | -2.24 (9.73) | -2.74 (11.77) | -2.36 (11.17) |
| | **Swing phase - peak ROM** (º) | | | | | |
| | Ankle * DF(+)/PF(-) | Cryotherapy first | 2.99 (5.39) | 1.28 (6.15)* | 2.01 (5.46) | 1.22 (5.52)* |
| | | Control first | 3.37 (4.57) | 1.81 (4.27)* | 5.04 (5.45) | 3.56 (5.89)* |
| | Knee * EXT(+)/FLEX(-) | Cryotherapy first | -35,51 (11.07) | -37.41 (12.29) | -36.43 (11.61) | -39.56 (13.47) |
| | | Control first | -44.53 (13.09) | -46.02 (13.96) | -45.57 (11.55) | -46.43 (12.98) |
| | Hip * FLEX(+)/EXT(-) | Cryotherapy first | 18.50 (10.19) | 20.99 (12.89) | 15.85 (7.00) | 18.47 (6.41) |
| | | Control first | 17.60 (9.71) | 17.93 (8.54) | 20.45 (10.19) | 20.63 (11.25) |
| **Spatio-temporal** | | | | | | |
| | **Stance time** (s) | Cryotherapy first | 1.03 (0.29) | 0.94 (0.21) | 0.97 (0.19) | 0.92 (0.20) |
| | | Control first | 0.85 (0.21) | 0.81 (0.22) | 0.88 (0.34) | 0.82 (0.24) |
| | **Swing time** (s) | Cryotherapy first | 0.56 (0.13) | 0.53 (0.11) | 0.51 (0.10) | 0.52 (0.13) |
| | | Control first | 0.46 (0.10) | 0.45 (0.10) | 0.48 (0.13) | 0.47 (0.11) |
| | **Stride length** (m) | Cryotherapy first | 0.77 (0.17) | 0.82 (0.15)* | 0.81 (0.17) | 0.85 (0.16) |
| | | Control first | 0.91 (0.20) | 0.93 (0.21) | 0.96 (0.17) | 0.99 (0.19)* |
| | **Walking speed** (m/s) | Cryotherapy first | 0.50 (0.17) | 0.58 (0.17)* | 0.57 (0.17) | 0.62 (0.20)* |
| | | Control first | 0.73 (0.24) | 0.78 (0.23)* | 0.76 (0.24) | 0.82 (0.27)* |
| | **Cadence** (steps/min) | Cryotherapy first | 81.21 (14.32) | 94.03 (27.14) | 85.62 (12.49) | 88.90 (15.02)* |
| | | Control first | 97.85 (18.71) | 101.47 (19.56)* | 96.35 (22.41) | 100.16 (23.56) |

Data expressed as mean (standard deviation). * $p<0.05$ compared to pre-intervention. Abbreviations: DF, Dorsiflexion; PF, Plantarflexion; EXT, Extension; FLEX, Flexion; ROM, Range Of Motion; s, seconds; m, meters; min, minutes.

**Discussion**

In this study, we examined whether cryotherapy (ice pack modality) applied to spastic plantarflexor muscles could affect spasticity level and angular/spatiotemporal gait parameters in subjects post-stroke immediately after application. In accordance with our initial hypothesis, the current findings showed that cryotherapy decreased the plantarflexor muscles spasticity level, while the improvement in gait performance was limited. Some differences were observed in the comparisons between pre and post assessments, however, it is important to highlight that such findings occurred regardless of intervention applied (control or cryotherapy). Furthermore, in general lines, changes are not clinically meaningful. For example, the increase observed in gait velocity, regardless of intervention, did not exceed typical minimal detectable change (MDC) for comfortable gait speed measurements for patients with pathology.[40] Interestingly, our findings showed that cryotherapy did decrease the plantarflexor tonus according to the Modified Ashworth Scale. However, it did not affect spatiotemporal parameters or ankle, knee and hip flexion/extension during gait, evaluated immediately after cryotherapy application, compared to control application. These findings provide important information regarding a technique still used in some rehabilitation centers and may help clinicians in their evidence-based approach to treating those post-stroke.

Studies have also shown a decrease in spasticity level following cryotherapy application in subjects with neurological injury, such as stroke and traumatic brain injury.[23, 41] Although the mechanisms involved in the spasticity response following this intervention are not completely elucidated, most of the evidence currently available suggests a positive effect, i.e. cryotherapy decreasing spasticity level as measured for example by the Modified Ashworth Scale (lower score after cryotherapy) or H-reflex latency (increase due to nerve conduction velocity reduction following cryotherapy).[21, 23, 41] However, there is a lack of evidence on whether cryotherapy would lead to an immediate improvement in gait pattern of subjects post-stroke, considering this decrease in the spasticity level following intervention.

The main and most innovative result of the current study is related to the immediate effects of cryotherapy on walking in those post-stroke. Regardless of a decrease in spasticity, measured at rest, no improvements were observed in spatiotemporal or angular (sagittal plane) gait variables post-cryotherapy, compared to control intervention. Unlike the commonly held belief of many clinicians, this study did not find a relationship between an immediate reduction in plantarflexor muscle spasticity and gait spatiotemporal or kinematic parameters. These findings provide important information regarding spasticity management when aiming at improving gait performance in those post-stroke.

Indeed, evidence for the relation between spasticity and gait impairments in persons post-stroke has been controversial.[5, 8, 18, 19] While some studies have shown that spasticity was a relevant factor that contributes to spatial and temporal asymmetry during gait,[8, 19] other studies did not provide evidence for this relationship.[5, 18] For example, a study showed no relation between spasticity, evaluated according to the MAS score, and sagittal ankle kinematics during gait among stroke survivors, such as peak dorsiflexion during swing and range of motion during stance.[5] Reports in other neurologic clinical populations have also demonstrated that spasticity has a limited association with walking dysfunction.[42-44] This poor or lack of association between spasticity and gait impairments may help explain the limited effect of cryotherapy on spatiotemporal and angular gait parameters in the current study, supporting the premise that spasticity seems not to be a major component contributing to gait impairment post-stroke. [5, 14]

Given the complexity of gait control and its changes following stroke[45], impairments other than spasticity should also be considered as factors that interfere with gait performance. For example, plantarflexor and dorsiflexor weakness is known as a limiting factor of gait speed and endurance in subjects post-stroke.[10, 46, 47] Thus, considering all of the body structure and function impairments that might negatively influence gait after stroke, it is not surprising that cryotherapy by itself was not able to improve gait parameters. Since this intervention aimed at minimizing the influence, if any, of spasticity on gait, one among many impairments post-stroke, our results suggest minimizing the focus on spasticity and instead considering placing more attention on the body structure and function impairments that have been convincingly shown to be related to poor gait function after stroke.

In accordance with the current findings, other techniques has been shown to be effective in reducing spasticity in patients post-stroke,[30, 31, 48] however their effectiveness in improving functional mobility is not well established and in most of the studies evidence is lacking.[30, 31] For example, a recent systematic review and meta-analysis concluded that botulinum toxin injection for lower limb spastic muscles is an effective treatment in reducing tonus post-stroke, but no improvement in gait speed was observed in botulinum toxin group compared to the control.[31] It seems, therefore, that the premise that spasticity should be addressed and managed by clinicians during gait rehabilitation post-stroke in order to reach functional gains must be seen with some limitations.

In summary, our findings showed that by decreasing plantarflexor spasticity, cryotherapy was not able to improve gait parameters in subjects post-stroke. These results have important clinical implications and might be helpful for researchers and clinicians regarding post-stroke gait rehabilitation. While it remains to be investigated in future studies if the association of cryotherapy and other techniques would have an effect on gait post-stroke, our findings shows that cryotherapy (ice pack) by itself, and therefore, a temporary decrease on spasticity level do not interfere directly on function gains. Given that gait is a complex task and following stroke a combination of many neural and biomechanical impairments may occur,[45] a broader approach should be considered, while case-by-case impairments and goals should also be taken into account.

Finally, the results of this study must be considered in the context of its limitations. The results of this study demonstrate the immediate effects of cryotherapy on spasticity and gait parameters in subjects with chronic hemiparesis post-stroke with mild or moderate spasticity. Future studies should evaluate a greater number of subjects with different levels of tonus increase and gait impairments, as well as in different phases post-stroke (i.e., subacute) to further understand the effects of cryotherapy on spastic patients with different characteristics. In addition, the results are limited to the effects of cryotherapy applied as ice pack modality, on spastic plantarflexor muscles. Our findings and conclusions should not be generalized to other cryotherapy modalities, such as cold water immersion, or to the application on other muscle groups, such as upper limb spastic muscles. It is also possible that the immediate effects of spasticity reduction of other lower limb muscles may have had a greater effect on gait parameters in those post-stroke. Furthermore, other gait parameters may be more sensitive to the cryotherapy effects, such as outcomes that indicate the variability within and between kinematic waveforms, which should be investigated in future studies. Focus on the plantarflexor muscles was chosen because of their established importance to walking function after stroke,[49, 50] however, it is possible that the reduction of spasticity in other muscles may have shown a different effect on gait parameters after stroke. More research is needed to clarify the effects of those interventions.

## Conclusion

Our results suggest that cryotherapy (ice pack modality), applied to spastic plantarflexor muscles, is effective in decreasing spasticity level according to the Modified Ashworth Score, but does not improve gait parameters such as spatiotemporal and sagittal angular variables in spastic chronic hemiparetic subjects post-stroke.

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# ESTUDO II

# Cryotherapy does not affect lower limb strength post-stroke: a randomized controlled study

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## Abstract

*Background and Purpose:* Cryotherapy is among the techniques applied to spastic muscles in neurological patients in order to temporarily reduce spasticity, aiming at facilitating muscle performance and ultimately functional training, such as walking. However, its effects on muscle capacity to generate strength have not been studied in subjects post-stroke. Thus, the aim of this study is to investigate the immediate effects of cryotherapy (ice pack modality), applied to spastic plantarflexors muscles of subjects post-stroke, on isometric, concentric and eccentric torque of plantarflexors and dorsiflexors. *Methods:* This is a randomized controlled crossover study. Sixteen chronic hemiparetic subjects participated in this study. Cryotherapy (ice pack) or Control (room temperature sand pack) were applied to the calf muscles of the paretic limb. Torque assessments were performed using an isokinetic dynamometer, before and immediately after intervention. *Results and Discussion:* Cryotherapy application did not change the isometric, concentric and eccentric response compared to control application. These findings contribute to the evidence-based approach in the clinical rehabilitation post-stroke. If the goal is to increase muscle capacity to generate force in the lower limbs post-stroke, cryotherapy (ice pack modality) seems to not be effective. On the other hand, it is important to highlight that cryotherapy did not decrease the capacity to generate force as well, and most likely would not negatively affect functionality post- application. *Conclusions:* The findings of this study suggest that cryotherapy (ice pack) applied to the calf muscles of subjects with chronic hemiparesis does not affect dorsiflexion or plantarflexion strength.


**Key-words:** Muscle Strength, Torque, Spasticity, Cold therapy, Stroke

**Introduction**

Stroke is currently considered one of the leading causes of disability in adults worldwide.[1, 2] Hemiparesis is a major motor impairment following stroke, affecting most stroke survivors , and is associated with significant functional mobility limitation and reduced social participation.[3] The motor dysfunctions often persist, affecting 65% of stroke survivors even after 1-year post neurological event.[4] Among these impairments observed post-stroke, ankle-related deficits are key factors that contribute to changes in functional mobility, such as gait. [5, 6] Muscle weakness is clinically recognized as one of the major limiting factors of functionality.[7] For example, dorsiflexor weakness is one of the main deficits interfering with gait velocity and temporal asymmetry post-stroke.[6]

Several factors can lead to this decrease in force generated by the plantar flexors and dorsiflexors of the ankle in the paretic limb, including neural[8, 9] and muscular components.[10-12] Previous studies have shown that spasticity of plantarflexors is negatively related to muscle strength in the lower extremities, showing that spastic muscles are more likely to be weaker post-stroke.[13] This relationship between those impairments had led to the rationale that probably the spasticity, as an abnormal tone, may hinder the development of voluntary muscle tone and therefore decrease the muscle capacity to generate strength.[13] Although this relationship does not mean causal effect and spasticity contribution for gait deficits are controversial in the literature,[5, 6, 14, 15] several interventions are still used in clinical practice in order to temporarily minimize spasticity.

One of the techniques used in some rehabilitation centers is cryotherapy.[16-19] The rationale is that it would lead to a temporarily reduce in spasticity, allowing the muscle to generate more strength, and ultimately optimizing functional training. Cryotherapy is defined as the application of any substance that draws heat from the body, resulting in decreased tissue temperature.[20] In healthy individuals, the physiological effects of cryotherapy include reduced blood flow and decreased local metabolism, as well as reduced speed of sensory and motor nerve conduction.[21, 22] However, even in healthy subjects, there is no consensus in the literature regarding the effect of cryotherapy on muscle performance. While some studies have shown an increase in torque generation following cryotherapy application, others observed no effects or even a decrease in muscle performance immediately after cooling. [23-26]

To the best of our knowledge, no studies have investigated the effects of cryotherapy on lower limbs torque generation of individuals with spastic hemiparesis. It is crucial to understand whether, and in which extent, cryotherapy application leads to positive, negative or no effects on muscle performance in order to guide clinicians on evidence-based approach. On one hand, cryotherapy applied on spastic muscles post-stroke could have a positive effect on strength capacity, most likely due to a decrease in muscle resistance to movement. On the other hand, it could actually lead to a decrease in muscle performance possibly due to an inhibition of neuromuscular transmission.[27] Alternatively, a combination of positive and negative physiological mechanisms could result in no effect in muscle strength post-stroke. Thus, the aim of this study was to investigate the immediate effects of cryotherapy (ice pack modality), applied to spastic plantarflexor muscles of subjects post-stroke on isometric, concentric and eccentric strength of ankle plantaflexion and dorsiflexion. We hypothesized that cryotherapy would have a limited effect on increasing muscle strength.

## Methods

### *Experimental Design Overview*

This study was a single-blinded, randomized controlled crossover trial, conducted with chronic hemiparetic subjects at a single center (Federal University of São Carlos - UFSCar, Brazil). Subjects were recruited from a variety of sources including the UFSCar rehabilitation center (São Carlos, SP, Brazil), the University Hospital of São Carlos (São Carlos, SP, Brazil) and through advertisements. The ethics Committee in Brazil approved the protocol (Number: 1.469.151) and the study was registered in the Clinical Trials (URL: http://www.clinicaltrials.gov. Unique identifier: NCT02736747). All participants provided written informed consent.

A schematic representation of the study experimental design is shown in Figure 1. Assessments were divided into three days. On the first day (Day 0), a screening assessment was performed to select the sample according to inclusion and exclusion criteria. On the same day, a clinical assessment was performed if the participant met the criteria. Then, enrolled subjects participated in a second session (Day 1), which consisted of an isokinetic dynamometer familiarization test. On this day, subjects performed isometric/isokinetic tests so that they could become familiar with the equipment. The purpose of this familiarization was to avoid the effects of learning that could interfere in the comparisons of the pre- and post-cryotherapy or control evaluations.[28] One week later, subjects underwent a third section (Day 2), when the actual isometric/isokinetic assessment was performed, before and immediately after intervention (Control or Cryotherapy). A wash-out period of fifteen days was considered and Day 1 and Day 2 were performed again, but at this time before and immediately after the other intervention (Control or Cryotherapy). Enrolled subjects were randomly assigned to one of two groups to receive Control intervention first (PL) or Cryotherapy Intervention first (CT). Sealed opaque envelopes prepared by an independent member of staff were used for randomization implementation.

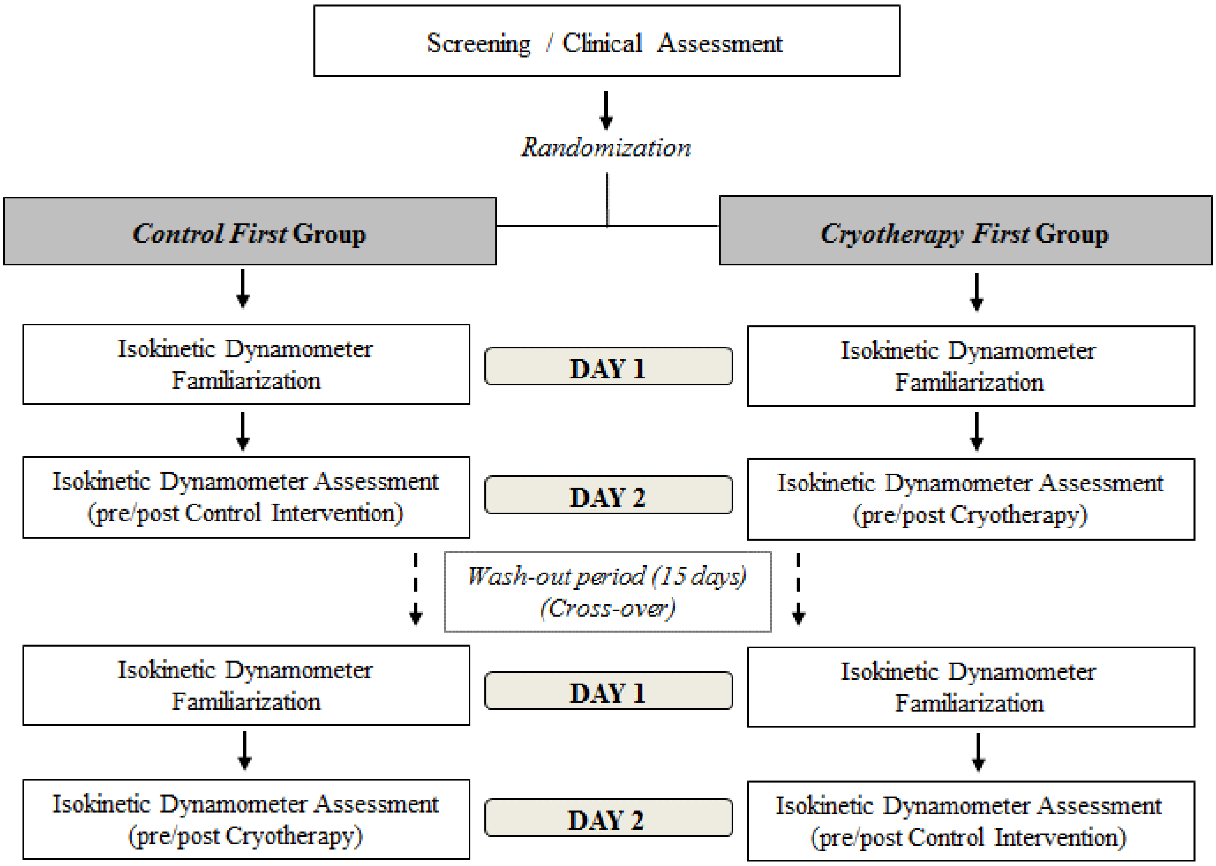


**Figure 1.** Experimental design of the study. Abbreviations: MAS, Modified Ashworth Scale.

*Participants*

The following inclusion criteria were considered: (1) chronic hemiparetic subjects (post-stroke time greater than 6 months) due to unilateral ischemic stroke of any hemispheres; (2) aged between 40 and 75 years; (3) spasticity levels between 1 and 3 according to MAS[29] on the ankle flexor muscles; (4) walking ability classified in levels 2, 3, 4 or 5 according to the Functional Ambulation Category (FAC)[30]; (5) minimum score on the Mini-Mental State Examination, according to the subject's educational level [31, 32].

The following exclusion criteria were considered: (1) peripheral neuropathy; (2) intolerance to the ice pack application; (3) presence of Raynaud's phenomenon; (4) ulcers or skin lesions; (5) serious cardiovascular or peripheral vascular disease (heart failure, arrhythmia or angina pectoris); (6) any other orthopedic or neurological disorder; botulinum toxin application up to six months before the study; (7) cognitive or communication disabilities; (8) lower limbs joint or previous muscle injuries; (9) pain during the assessment procedures.

*Clinical assessment*

In order to characterize the subjects enrolled in this study, a clinical evaluation was carried out, which included 1) collection of personal data, such as age and stroke related information; 2) collection of anthropometric data, such as weight and height; 3) evaluation of lower-limb sensorimotor impairment according to the Fugl Meyer Scale [33]; 4) passive range of motion (ROM) for dorsiflexion and plantar flexion using a goniometer (the goniometry was performed with the patient sitting on a stretcher, with their leg suspended and knee in a neutral position at 90° flexion).

*Isokinetic dynamometer evaluation protocol*

For the dorsiflexor and plantarflexor isometric and isokinetic evaluations, a Biodex System III isokinetic dynamometer was used, which was calibrated before each evaluation according to the manufacturer's instructions. During the evaluation, individuals remained seated in a chair, with the hip at 70° and knee at 45° of flexion, with crossbelts stabilizing the trunk. Likewise, the hip and thigh were firmly attached to the dynamometer chair. The dynamometer rotation axis was aligned with the lateral malleolus and the foot was positioned and secured with strips on the device designated for ankle joint.

The isometric evaluation was performed with the ankle in the neutral position.[34] To test the dorsiflexor muscles, the subject was instructed to lift the tip of the foot and maintain maximum contraction for 10 seconds. For the plantar flexors, the subject was instructed to push the tip of the foot toward and to maintain maximum contraction for 10 seconds. For the isokinetic evaluation, maximum contractions in the dorsiflexion and plantar ankle flexion movements at 30 °/s were obtained in the concentric and eccentric modes. [5, 35] The ROM was set between 10° of dorsiflexion and 20° of plantar flexion. Before each test, the subjects performed three repetitions of the movements of dorsiflexion and plantar flexion, with submaximal resistance, in order to become familiar with the movement. Subsequently, the subjects performed five successive maximum contractions, [36] during which verbal commands were given by the evaluator asking the subjects to push and pull the lever with the greatest possible force throughout the ROM. The order in which the concentric or eccentric tests were performed was randomized. Cardiac parameters (blood pressure and heart rate) were monitored before, during and at the end of each evaluation. In addition, subjects were instructed and monitored to not perform a valsalva maneuver during strength tests. All data were processed using Matlab software (The MathWorks, Natick, Massachusetts).

*Interventions*

All assessments were performed by the same experienced physiotherapist, who was blinded to intervention applied, whereas the intervention applications were performed by another research team member. Participants were instructed to avoid intake of stimulants such as alcohol, caffeine and chocolate 2 hours before the intervention and not exercising for at least 4 hours beforehand.[27] All procedures were performed from 2pm to 6pm in order to minimize the possible effects of the circadian rhythm. The room temperature was controlled at 25ºC in all procedures, and subjects had a period of 15 minutes for acclimatization at the beginning of assessments/intervention sessions.[22]

A rectangular area was defined to delimitate where the pack was placed as described by Herreira.[27] For the cryotherapy intervention, the pack (25 x 35cm) was filled with 1000g of crushed ice tied around the leg using a non-compressive elastic band[15]. For the control intervention, the pack was filled with 1000 g of sand, at room temperature so that the pressure was similar to the ice pack in order to prevent any variables besides temperature interfering with the analysis.

The participants were positioned in a comfortable chair for the intervention application. The leg was involved by a strap of plastic film, avoiding direct contact between the skin and the pack. Then, the pack (cryotherapy - ice; control - sand) was placed over the delimited area and maintained for 20 minutes. The subjects remained with the limb resting and neither ice nor sand was added during the application time.

*Data Analysis*

The sample size was calculated using using G.Power 3.1 software.[37] Pilot data from four subjects from the Cryotherapy First group and four from the Control First group were considered. The outcome used for this calculation was the isometric mean torque for dorsiflexors. The effect size of interaction (partial eta) was 0.379. The F-test (repeated measures ANOVA, within and between factors) was used, considering a power of 0.95 and alpha of 0.05. In addition, a loss of 20% of the data was considered, requiring a total sample size of 8 subjects.

The following outcomes were considered for analysis: 1) Isometric test: plantar flexors and dorsiflexors peak torque, mean torque, coefficient of variance (standard deviation of the obtained torque measures divided by their mean); 2) Concentric test: plantar flexor and dorsiflexor peak torque, total work and power; 3) Eccentric test: plantar flexor and dorsiflexor peak torque, total work and power. For all isometric, concentric and eccentric data, a mixed two-way ANOVA with repeated measures with Bonferroni's correction was used to verify the effect of interaction (group and evaluation time), evaluation time (before and after cryotherapy and control interventions) and group (cryotherapy first and control first). Partial $\eta^2$ is presented and a value of 0.2, 0.5, and 0.8 corresponds to a small, medium, and large effect.[38] A significance level of 0.05 was considered and all statistical tests were performed using SPSS software, version 17.0 (SPSS Inc., Chicago, IL, USA).

## Results

*Participants*

Four hundred and twenty nine subjects from the local community in São Carlos, SP (Brazil) were assessed for eligibility. From these subjects, 16 met the criteria and were enrolled in the study. They were randomly allocated to the Control First Group (n=9) or Cryotherapy First Group (n=7). All participants completed the experimental procedures, however some participants did not perform isometric, concentric and/or eccentric tests for dorsiflexion since they were not able to unlock the lever and start the test by themselves (Figure 2). No adverse effects were observed during data collection.

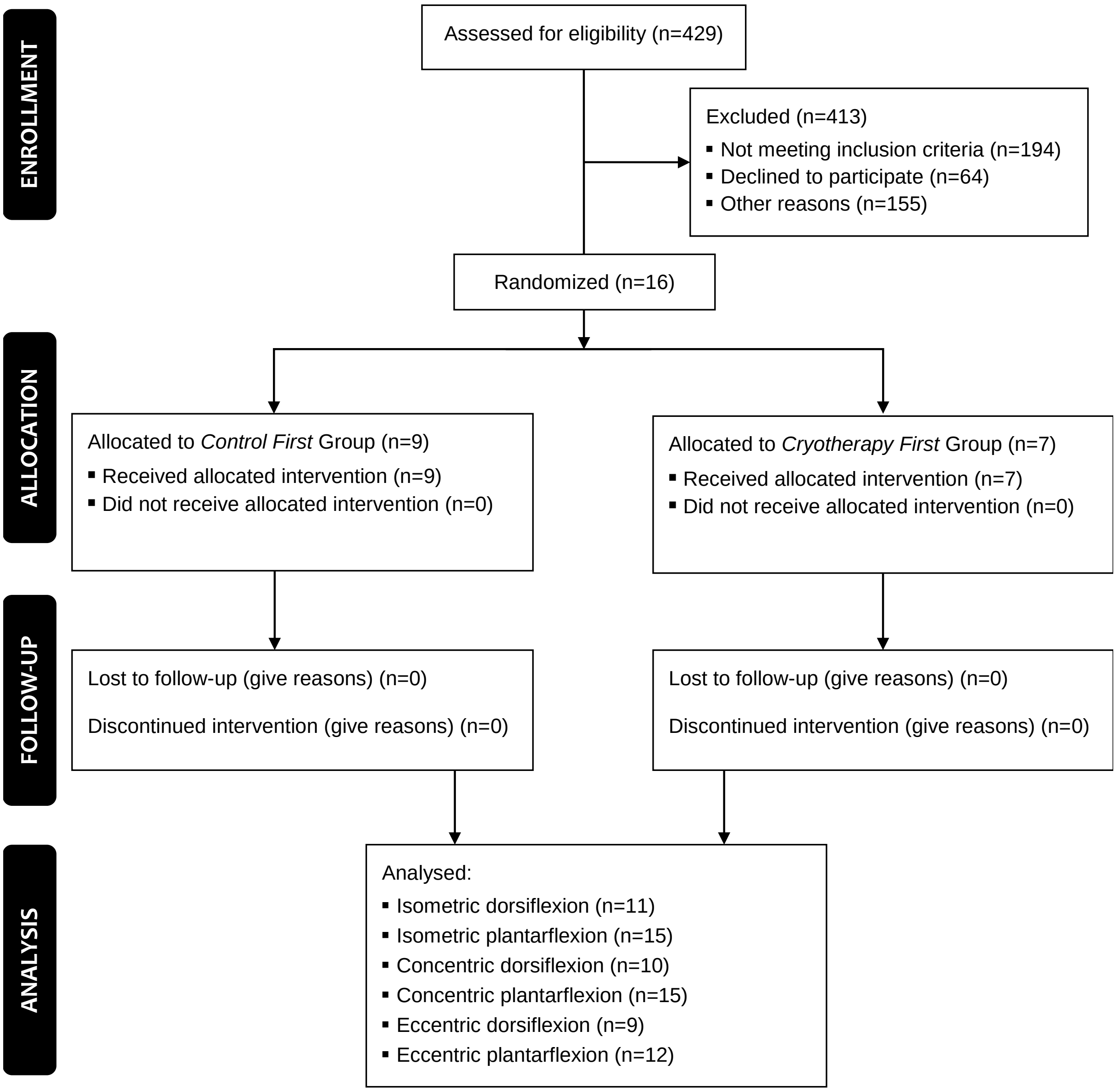


**Figure 2.** Flow diagram of study.

Characteristics of the participants are presented in Table 1. The mean age was 62 years old. The dominant side was the right one before stroke for all subjects. Regarding stroke-related characteristics, the stroke occurred in the right hemisphere in 6 subjects, whereas 9 subjects had a stroke in the left hemisphere. The time post-stroke was 29 months on average. In relation to plantarflexor muscle tone during baseline, ten participants presented a score 1+, five individuals a score 2 and 1 individual a score 3 on the MAS. The mean of the comfortable walking speed was 0.77 m/s.

**Table 1.** Sample characterization

| *Outcomes* | *Values* |
|---|---|
| Age (years) | 62.3 (52-71) |
| Gender (F/M) | 2/14 |
| Dominant side (R/ L) | 15/0 |
| Hemiparesis Side (R/L) | 9/6 |
| Time post-stroke (months) | 29 (20-135) |
| MAS of ankle plantar flexors muscles (0/1/1+/2/3/4) | (0/0/10/5/1/0) |
| FMA-LE, total score | 81 (65-98) |
| FMA-LE, subscale score of sensibility | 11 (4-12) |
| FMA-LE, subscale score of motor function | 21 (13-34) |
| Comfortable Walking Speed (m/s) | 0.77 (±0.24) |

Abbreviations: F, Female; M, Male; R, Right; L, Left; MAS, Modified Ashworth Scale; FMA-LE, Fugl-Meyer Assessment - Lower Extremity. Data expressed as mean (minimum-maximum), except FMA-LE, expressed as median (minimum-maximum), Comfortable Walking Speed as mean (standard deviation) and MAS, expressed as number of subjects in each category/score.

*Cryotherapy effect on isometric, concentric and eccentric strength*

Overall, cryotherapy did not interfere with the ability to generate dorsiflexion or plantarflexion strength (Table 2). There was no statistically significant interaction between the group (cryotherapy first/control first) and evaluation time (pre/post intervention) for all isometric, concentric and eccentric variables assessed ($p>0.05$). Furthermore, there was no group effect on any outcomes ($p>0.05$), demonstrating that the order of intervention (cryotherapy first or control first) did not influence the results. No differences were observed between pre-intervention in the first block of evaluation/treatment and pre-intervention in the second block ($p>0.05$), regardless of the group (cryotherapy first or control first), confirming that the baseline measurements were similar. An overview of the results of mixed two-way ANOVA for all variables are presented in the supplementary material (Table S1).

The main effect of evaluation time (pre/post cryotherapy or control intervention) showed that there was no difference among evaluation time points for all variables in dorsiflexion isometric assessment, dorsiflexion and plantarflexion concentric assessments and dorsiflexion and plantarflexion eccentric assessments. Although there was a significant effect of the evaluation time for peak torque ($F=4.142$, $p=0.014$, partial $\eta^2=0.293$) and mean torque ($F=3.657$, $p=0.023$, partial $\eta^2=0.268$) during plantarflexion isometric assessment, no differences were observed in pairwise comparisons between pre and post intervention ($p>0.05$), regardless of the intervention used (cryotherapy or control).

**Table 2.** Dorsiflexor and plantarflexor isometric, concentric and eccentric outcomes (paretic side) for the Cryotherapy First group and Control First group, pre and post interventions (control or cryotherapy).

| *Muscle group* | *Measure* | *Group* | *Intervention* – *Cryotherapy* Pre | *Cryotherapy* Post | *Control* Pre | *Control* Post |
|---|---|---|---|---|---|---|
| **Dorsiflexor** | **Isometric** | | | | | |
| | Peak torque (N.m) | Cryotherapy first | 12.70 (5.65) | 13.85 (5.07) | 10.45 (5.15) | 10.45 (3.18) |
| | | Control first | 13.36 (6.70) | 10.69 (6.02) | 10.54 (3.70) | 10.41 (3.25) |
| | Average torque (N.m) | Cryotherapy first | 5.06 (5.21) | 7.48 (3.96) | 5.80 (5.17) | 4.39 (2.08) |
| | | Control first | 9.03 (6.74) | 6.17 (6.91) | 6.51 (3.09) | 5.98 (3.01) |
| | Coefficient of Variance (%) | Cryotherapy first | 2.28 (2.39) | 3.71 (4.21) | 2.94 (3.95) | 1.47 (0.95) |
| | | Control first | 3.80 (2.50) | 2.75 (2.69) | 3.67 (2.70) | 3.07 (1.91) |
| | **Concentric** | | | | | |
| | Peak torque (N.m) | Cryotherapy first | 6.00 (4.48) | 5.13 (3.79) | 7.17 (4.67) | 4.86 (3.23) |
| | | Control first | 4.50 (3.18) | 3.98 (3.35) | 6.11 (4.47) | 5.70 (4.96) |
| | Total Work (J) | Cryotherapy first | 9.42 (8.10) | 8.38 (6.68) | 11.79 (9.45) | 7.41 (6.10) |
| | | Control first | 5.73 (5.18) | 5.49 (6.22) | 9.65 (8.97) | 8.96 (11.00) |
| | Power (W) | Cryotherapy first | 9.81 (8.18) | 8.16 (7.19) | 12.12 (8.85) | 7.81 (5.93) |
| | | Control first | 5.96 (4.81) | 5.54 (5.69) | 10.12 (10.09) | 9.32 (11.62) |
| | **Eccentric** (°) | | | | | |
| | Peak torque (N.m) | Cryotherapy first | 27,13 (9,49) | 23,98 (9,58) | 27,50 (9,26) | 26,57 (6,46) |
| | | Control first | 27,61 (5,53) | 24,16 (3,66) | 24,25 (8,96) | 23,98 (8,70) |
| | Total Work (J) | Cryotherapy first | 60,38 (27,98) | 50,23 (28,59) | 54,87 (32,49) | 62,67 (12,17) |
| | | Control first | 66,05 (21,60) | 52,91 (17,90) | 58,85 (34,81) | 53,71 (35,53) |
| | Power (W) | Cryotherapy first | 66,01 (22,09) | 55,15 (25,80) | 64,68 (24,61) | 67,05 (15,99) |
| | | Control first | 68,25 (15,76) | 59,34 (10,64) | 60,97 (25,20) | 59,16 (26,37) |
| **Plantar Flexor** | **Isometric** | | | | | |
| | Peak torque (N.m) | Cryotherapy first | 29.64 (12.09) | 30.99 (3.77) | 36.13 (19.29) | 35.77 (20.18) |
| | | Control first | 38.09 (15.48) | 38.41 (3.69) | 38.26 (13.78) | 44.46 (21.49) |
| | Average torque (N.m) | Cryotherapy first | 25.10 (10.00) | 27.13 (14.59) | 29.53 (14.48) | 29.33 (15.80) |
| | | Control first | 30.50 (12.16) | 31.56 (12.07) | 31.57 (10.92) | 38.58 (18.09) |
| | Coefficient of Variance (%) | Cryotherapy first | 11.77 (7.94) | 11.69 (7.13) | 11.15 (10.99) | 12.35 (9.82) |
| | | Control first | 5.15 (2.10) | 7.45 (4.46) | 9.76 (5.24) | 12.98 (7.87) |
| | **Concentric** | | | | | |
| | Peak torque (N.m) | Cryotherapy first | 14.05 (4.84) | 14.42 (6.70) | 17.01 (8.44) | 16.48 (8.01) |
| | | Control first | 22.84 (12.73) | 26.07 (16.28) | 23.27 (16.10) | 24.52 (17.59) |
| | Total Work (J) | Cryotherapy first | 32.32 (14.30) | 31.92 (17.38) | 36.99 (20.90) | 33.24 (20.91) |
| | | Control first | 50.75 (33.50) | 58.15 (40.79) | 53.16 (45.11) | 53.57 (47.32) |
| | Power (W) | Cryotherapy first | 34.11 (14.26) | 33.46 (16.70) | 40.45 (21.79) | 38.86 (18.95) |
| | | Control first | 53.91 (30.15) | 61.88 (35.81) | 55.46 (39.36) | 58.36 (42.67) |
| | **Eccentric** (°) | | | | | |
| | Peak torque (N.m) | Cryotherapy first | 46.54 (11.50) | 44.51 (25.70) | 49.38 (24.56) | 47.94 (22.00) |
| | | Control first | 52.95 (24.25) | 47.04 (20.48) | 51.51 (26.26) | 54.66 (27.26) |
| | Total Work (J) | Cryotherapy first | 79.40 (24.93) | 79.67 (47.42) | 99.36 (40.47) | 97.67 (33.44) |
| | | Control first | 93.44 (44.02) | 89.49 (41.07) | 99.06 (50.33) | 97.81 (63.85) |
| | Power (W) | Cryotherapy first | 85.74 (22.35) | 84.74 (47.10) | 97.62 (41.14) | 96.94 (38.39) |
| | | Control first | 94.02 (34.75) | 92.96 (33.24) | 100.41 (41.77) | 101.96 (48.85) |

Data expressed as mean (standard deviation).

**Table 1S**. Overview of the results of mixed two-way ANOVA for isometric, concentric and isometric outcomes for paretic limb dorsiflexor and plantarflexor.

| | | Effect of Evaluation | | | | Effect of Evaluation X Group | | | | Effect of Group | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| ***Muscle group*** | ***Measure*** | df | F | P value | Partial $\eta^2$ | df | F | P value | Partial $\eta^2$ | df | F | P value | Partial $\eta^2$ |
| **Dorsiflexor** | **Isometric** | | | | | | | | | | | | |
| | Peak torque | 3 | 0.382 | 0.767 | 0.041 | 3 | 1.564 | 0.221 | 0.148 | 1 | 0.060 | 0.812 | 0.007 |
| | Average torque | 1.547 | 0.776 | 0.448 | 0.079 | 1.547 | 0.964 | 0.383 | 0.097 | 1 | 0.156 | 0.702 | 0.017 |
| | Coefficient of Variance | 3 | 2.434 | 0.087 | 0.213 | 3 | 1.489 | 0.240 | 0.142 | 1 | 0.211 | 0.657 | 0.023 |
| | **Concentric** | | | | | | | | | | | | |
| | Peak torque | 1.273 | 1.291 | 0.296 | 0.139 | 1.273 | 0.474 | 0.552 | 0.056 | 1 | 0.101 | 0.759 | 0.012 |
| | Total Work | 1.255 | 0.889 | 0.393 | 0.100 | 1.255 | 0.434 | 0.569 | 0.051 | 1 | 0.184 | 0.679 | 0.023 |
| | Power | 1.172 | 0.984 | 0.361 | 0.110 | 1.172 | 0.394 | 0.578 | 0.047 | 1 | 0.168 | 0.692 | 0.021 |
| | **Eccentric** | | | | | | | | | | | | |
| | Peak torque | 3 | 0.495 | 0.690 | 0.076 | 3 | 0.682 | 0.575 | 0.102 | 1 | 0.231 | 0.648 | 0.037 |
| | Total Work | 3 | 0.454 | 0.718 | 0.070 | 3 | 0.302 | 0.823 | 0.048 | 1 | 0.010 | 0.924 | 0.002 |
| | Power | 3 | 0.317 | 0.813 | 0.050 | 3 | 0.345 | 0.793 | 0.054 | 1 | 0.108 | 0.754 | 0.018 |
| **Plantar Flexor** | **Isometric** | | | | | | | | | | | | |
| | Peak torque | 3 | 4.142 | 0.014 | 0.293 | 3 | 1.443 | 0.250 | 0.126 | 1 | 0.128 | 0.728 | 0.013 |
| | Average torque | 3 | 3.657 | 0.023 | 0.268 | 3 | 0.939 | 0.434 | 0.086 | 1 | 0.131 | 0.725 | 0.013 |
| | Coefficient of Variance | 1.381 | 1.189 | 0.314 | 0.106 | 1.381 | 0.953 | 0.377 | 0.087 | 1 | 0.676 | 0.430 | 0.063 |
| | **Concentric** | | | | | | | | | | | | |
| | Peak torque | 1.614 | 1.117 | 0.335 | 0.085 | 1.614 | 1.420 | 0.262 | 0.106 | 1 | 1.573 | 0.234 | 0.116 |
| | Total Work | 1.347 | 0.433 | 0.578 | 0.035 | 1.347 | 0.820 | 0.413 | 0.064 | 1 | 1.137 | 0.307 | 0.087 |
| | Power | 1.495 | .931 | 0.386 | 0.072 | 1.495 | 1.456 | 0.255 | 0.108 | 1 | 1.576 | 0.233 | 0.116 |
| | **Eccentric** | | | | | | | | | | | | |
| | Peak torque | 3 | 0.474 | 0.703 | 0.050 | 3 | 0.779 | 0.516 | 0.080 | 1 | 0.000 | 1.000 | 0.000 |
| | Total Work | 1.307 | 0.799 | 0.422 | 0.082 | 1.307 | 0.325 | 0.638 | 0.035 | 1 | 0.001 | 0.978 | 0.000 |
| | Power | 1.412 | 0.991 | 0.369 | 0.099 | 1.412 | 0.318 | 0.659 | 0.034 | 1 | 0.000 | 0.999 | 0.000 |

**Discussion**

This study investigated the immediate effects of cryotherapy (ice pack modality) on ankle plantarflexion and dorsiflexion isometric and isokinetic strength in subjects with chronic spastic hemiparesis. Our findings show that this intervention did not interfere with the subjects' capacity to generate isometric, concentric or eccentric torque, which is in accordance with our initial hypothesis that cryotherapy would have a limited effect on increasing muscle strength. These findings provide important evidence regarding cryotherapy effects (ice pack) on lower limb muscular performance post-stroke.

Considering the negative relationship between spasticity, muscle performance[13] and gait parameters,[5, 6] techniques are still used in some rehabilitation centers targeting a decrease in spasticity in order to optimize movement ability and ultimately improve function. Interestingly, the capacity to generate strength was not affected by cryotherapy application when compared to control application in this study, even though a decrease in plantarflexor spasticity according to the Modified Ashworth Scale score occurred following cryotherapy (data not shown). It seems, therefore, that other factors rather than spasticity play a more important role in plantarflexor and dorsiflexor force generation capacity post-stroke. Indeed, it is well known that several factors can lead to this decrease in force generated by the plantar flexors and dorsiflexors of the ankle in the paretic limb, including neural[8, 9] and muscular components.[10-12] Among all of them, voluntary activation failure is described as the main impairment related to muscle weakness of the plantar flexors [9] and dorsiflexors.[8] Therefore, it is not surprising that cryotherapy alone applied to the calf muscles was not able to improve the muscle capacity to generate force.

Accordingly, a previous study[18] evaluated the immediate effect of cryotherapy (ice pack) on reflex excitability and voluntary muscle activity in subjects with chronic hemiparesis. Although changes favorable to decrease in spasticity such as increased H-reflex latency were observed, these alterations were not enough to modify the activation pattern of the tibialis anterior after application of cryotherapy on calf muscles. Taken together, these previous findings along with the current results show that, regardless of a decrease in spasticity, cryotherapy (ice pack) applied to the calf muscles of subjects with chronic spastic hemiparesis has no effects on muscle contractile capacity or force generation capacity.

Unfortunately, comparisons of the current results and previous findings from studies in healthy subjects are limited, which could contribute to the understanding of cooling effect mechanisms. Although cryotherapy has been widely studied in healthy subjects aiming at elucidating its effects on muscle performance, controversial results are observed. [23-26] These disparities appear to be related to differences in the cold modalities used, the location of cryotherapy application (muscles/joints) and the type of test performed to assess muscle performance. A previous study, however, did investigate the effect of cryotherapy on muscle performance in healthy subjects using a similar application protocol to the one used in the current study and allow a more reliable comparison.[24] A decrease in concentric peak torque of plantarflexors was observed following ice pack application on the calf muscles, which was attributed to a inhibition of neuromuscular transmission, while an increase in plantaflexor isometric peak torque was observed.[24] These findings are not in agreement with the present study results.

Some hypothesis might explain the different results and the absence of changes in muscle performance following cryotherapy in the current study. There is evidence showing that the response to cooling is velocity-dependent, i.e., isokinetic contractions performed at higher velocities have been shown to be more affected than lower velocities in healthy subjects.[39, 40] In the present study, both concentric and eccentric modes were tested at a relatively low velocity (30°/s), which was chosen taking into account the maximum angular ankle velocity during normal walking.[5, 41] Therefore, it is possible that this could partially explain the absence of torque changes following cryotherapy in the present study and the discrepancies in results compared to the previous study in healthy subjects, in which higher velocities were tested (60°/s and 120°/s).[24] Regarding the increase in isometric plantarflexor torque following cryotherapy in the previous study with healthy subjects, the authors discuss that possibly, in response to the inhibition caused by cooling, a higher threshold motor unit was recruited as a compensatory mechanism. It is not surprising, therefore, that no increases in torque were observed in the current study following cryotherapy. The deficit in motor control and inability to appropriately recruit more motor units post-stroke[8, 9] might explain the absence of increase in torque generation in the present study.

*Clinical implications*

These findings provide important information regarding lower limb cryotherapy effects on force generation capacity in subjects with chronic spastic hemiparesis post-stroke. The understanding that the strength capacity was not affected, for either cooling muscles (plantarflexors) or antagonist muscles (dorsiflexors), may help clinicians and researchers in rehabilitation planning. On one hand, the results of this study suggest that if the goal is to increase muscle capacity to generate force in lower limbs post-stroke, cryotherapy (ice pack modality) does not seem to be effective. In fact, this intervention did not improve walking parameters, regardless of the decrease in spasticity (data not shown), reinforcing that the management of spasticity aiming at improving force generation in order to reach functional gains during gait rehabilitation post-stroke must be seen with some limitations. On the other hand, it is important to highlight that cryotherapy did not decrease the capacity to generate force, which could lead to negative effects during functional tasks. Taken together, these findings might contribute to the evidence-based approach in the clinical rehabilitation post-stroke. However, the effects of cryotherapy associated with other interventions, for example, kinesiotherapy following cryotherapy, were not evaluated in this study and should be addressed in future research studies to confirm its responses.

### *Study limitations*

The findings of this study show the immediate effects of cryotherapy on dorsiflexion and plantarflexion strength in ambulatory subjects with chronic hemiparesis post-stroke. Future studies should evaluate a greater number of subjects in different stages post-stroke (e.g., subacute) and with different functionality levels. Furthermore, the results and conclusions of this study specifically address the response to cryotherapy in subjects with mild or moderate spasticity and should not be generalized to subjects with more severe tonus alterations. Finally, the results are limited to the effects of ice pack modality applied to calf spastic muscles. Other studies are needed to confirm if the same responses would be seen following other cryotherapy modalities, such as cold water immersion, or to the application to other muscle groups, such as upper limb spastic muscles.

## Conclusion

The findings of this study suggest that cryotherapy (ice pack) applied to the calf muscles of subjects with chronic hemiparesis does not affect dorsiflexion or plantarflexion strength during isometric, concentric and eccentric contractions.

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# CONSIDERAÇÕES FINAIS

Os estudos apresentados nesta Tese de Doutorado abordaram os efeitos da crioterapia (pacote de gelo) em membros inferiores de indivíduos com hemiparesia espástica crônica pós-AVE. De um modo geral, os resultados sugerem que essa intervenção aplicada sobre os flexores plantares destes indivíduos parece ser uma técnica eficaz para reduzir o tônus muscular, mensurado clinicamente, mas não afeta o desempenho muscular e o padrão de marcha dos mesmos. Portanto, esses achados confirmam a efetividade do uso clínico da crioterapia se o objetivo da conduta é a diminuição do tônus muscular em indivíduos com hemiparesia espástica crônica pós-AVE. Por outro lado, o uso desta técnica na prática clínica deve ser considerado no contexto das limitações dos seu efeitos. Tal intervenção não apresentou efeitos, positivos ou negativos, sobre a capacidade da musculatura espástica (flexores plantares) ou antagonista (dorsiflexores) em gerar força, tampouco levou a modificações na marcha, independentemente da diminuição do tônus muscular dos sujeitos avaliados nestes estudos. Tais achados reforçam que o gerenciamento da espasticidade com o objetivo de melhorar o desempenho muscular e de otimizar a função durante a reabilitação da marcha pós-AVE deve ser visto com limitações. Assim, os resultados dos estudos apresentados fornecem informações importantes sobre os efeitos da crioterapia, uma técnica frequentemente utilizada durante o processo de reabilitação neurológica, podendo contribuir para uma abordagem baseada em evidências na prática clínica com pacientes pós-AVE.

## ATIVIDADES DESENVOLVIDAS NO PERÍODO

Durante o doutorado, tive a oportunidade de participar em atividades de pesquisa, ensino e extensão, concomitantes ao desenvolvimento do estudo que deu origem a esta tese. Participei como colaboradora de outros projetos de pesquisa, como os estudos intitulados "*Os efeitos da terapia robótica sobre a cinemática da marcha de indivíduos hemiparéticos crônicos: um ensaio clínico randomizado*" e "*Validade e confiabilidade da plataforma para monitoramento de atividades em reabilitação (MARe) em indivíduos pós Acidente Vascular Cerebral*", ambos ainda em andamento no Departamento de Fisioterapia da UFSCar. Ainda, a colaboração com outros pesquisadores do Laboratório de Pesquisa em Fisioterapia Neurológica (LAFiN) deu origem ao manuscrito intitulado "*Cryotherapy reduces muscles spasticity, but does not affect proprioception in ischemic stroke: a randomized sham-controlled crossover study*" submetido ao periódico *American Journal of Physical Medicine & Rehabilitation*; ao manuscrito "*Decreased brain-derived neurotrophic factor serum concentrations in chronic post-stroke subjects*", publicado no periódico *Journal of Stroke and Cerebrovascular Diseases* (2016); e ao manuscrito "*Post-stroke BDNF concentration changes following physical exercise: a systematic review*", em fase de submissão. Além disso, em colaboração com a Dra. Maíra Carolina Lixandrão e a Dra. Christiane Lanatovitz Prado-Medeiros, publicamos os capítulos de livro intitulados "*Strength training applied to Neurorehabilitation*" e "*Gait Training in Neurological Rehabilitation*" (In: Cleber Ferraresi. Physical Exercises: An Important Tool for Physical Therapy. 1ed. Hauppauge, NY: Nova Science Publishers, Inc., 2015).

Em 2014, participei do congresso e curso de análise de marcha (*Gait Course)* do "*1st Clinical Movement Analysis World Conference"* – Roma, Itália. Os resultados do estudo piloto inicialmente realizado durante o doutorado foram apresentados como pôster (Título: "*Cryotherapy decreases plantar flexors spasticity without changes in isometric strength in chronic stroke subjects: a pilot study*") no *9th World Congress for NeuroRehabilitation*, Philadelphia, EUA (2016). Participei também como coautora do trabalho intitulado "*Acute High-Intensity Exercise and Locomotor Adaptation After Stroke*" apresentado em formato de pôster no *American Society of Neurorehabilitation (ASNR) - 2017 Annual Meeting*, e o trabalho "*Effect of Acute Cardiovascular Exercise on Locomotor Adaptation and Learning After Stroke*" apresentado como *oral communication* no *Combined Sections Meeting (CSM) - 2017*. Além disso, durante este período, até a presente data, participo como revisora dos seguintes periódicos: *Topics in Stroke Rehabilitation, Brazilian Journal of Physical Therapy, BMC Neurology, Lasers in Surgery and Medicine, Disability and Rehabilitation*.

Ainda neste período participei como monitora de disciplinas da graduação em Fisioterapia da UFSCar pelo Programa de Estágio Supervisionado de Capacitação Docente (PESCD) e fui supervisora voluntária do estágio clínico em Fisioterapia Neurológica do curso de graduação da Fisioterapia da UFSCar. Participei também do projeto de extensão desenvolvido pelo Laboratório de Pesquisa em Fisioterapia Neurológica (LAFiN) intitulado "*Grupo terapêutico para indivíduos hemiparéticos crônicos*", realizado na Unidade Saúde Escola da UFSCar. Tive a oportunidade ainda de ministrar palestras em reuniões científicas realizadas na UFSCar, bem como de ser banca examinadora de trabalhos de conclusão de curso da graduação em Fisioterapia da UFSCar e do Curso de Especialização em Envelhecimento e Saúde da Pessoa Idosa da UFSCar. Fui co-orientadora de trabalhos de conclusão de curso e iniciação científica das alunas de Graduação em Fisioterapia da UFSCar Julia Blanco (Título: *Relação entre a cinemática do tornozelo durante a marcha, força muscular e espasticidade em indivíduos hemiparéticos crônicos*), Paula Fernanda Sávio Ribeiro (Título: *Efeito imediato da crioterapia sobre a cinemática do joelho durante a marcha de indivíduos hemiparéticos espásticos crônicos*), Lucilene Maria de Oliveira (Título: *Relação entre a resistência passiva ao alongamento e a força de dorsiflexores e flexores plantares após aplicação de crioterapia em indivíduos hemiparéticos espásticos crônicos*). Fui também orientadora do aluno Bruno Leonardo da Silva Gruninger no trabalho de conclusão do Curso de Especialização em Envelhecimento e Saúde da Pessoa Idosa da UFSCar (Título: *O que funciona em prevenção de quedas em idosos com doença de Parkinson? Uma revisão sistemática*).

Em 2016, fui contemplada com uma bolsa de estágio de pesquisa no exterior (BEPE – FAPESP), que me proporcionou a oportunidade de dar continuidade ao estudo sobre aspectos relacionados ao processo de reabilitação de indivíduos hemiparéticos crônicos. O estágio foi realizado no Laboratório de Comportamento Neuromotor (*Neuromotor Behavior Lab – NBL*) da *University of Delaware* (USA), sob supervisão da Profª Drª Darcy Reisman. Durante este período desenvolvi um estudo que teve como objetivo principal determinar se a introdução de perturbações graduais ou abruptas durante o aprendizado locomotor afeta a resposta de adaptação e a transferência de aprendizagem para a marcha sobre o solo em indivíduos pós-AVE. Este estudo deu origem a dois manuscritos. O primeiro manuscrito intitulado "*Different Error Size During Locomotor Adaptation Affects Transfer To Over Ground Walking Post-Stroke*" foi submetido ao periódico *Neurorehabilitation and Neural Repair* (Anexo V, número de submissão: NNR-17-0368). Um segundo manuscrito está em fase de análise dos dados e tem como objetivo o entendimento das alterações cinemáticas dos membros inferiores e tronco durante o aprendizado locomotor em indivíduos pós-AVE. Ainda, colaborei com outros projetos desenvolvidos neste período sob supervisão da Profª Darcy Reisman e Profª Susanne Morton, que resultará em participação como co-autora no manuscrito atualmente em fase de conclusão.

# ANEXOS

## Anexo I

UNIVERSIDADE FEDERAL DE
SÃO CARLOS/UFSCAR

**PARECER CONSUBSTANCIADO DO CEP**

**DADOS DA EMENDA**

**Título da Pesquisa:** EFEITOS IMEDIATOS DA CRIOTERAPIA SOBRE O DESEMPENHO NEUROMUSCULAR DA ARTICULAÇÃO DO TORNOZELO E O PADRÃO DA MARCHA DE INDIVÍDUOS HEMIPARÉTICOS ESPÁSTICOS CRÔNICOS PÓS-AVC

**Pesquisador:** Carolina Carmona de Alcântara

**Área Temática:**

**Versão:** 1

**CAAE:** 31637014.0.0000.5504

**Instituição Proponente:** Centro de Ciências Biológicas e da Saúde

**Patrocinador Principal:** FUNDACAO DE AMPARO A PESQUISA DO ESTADO DE SAO PAULO

**DADOS DO PARECER**

**Número do Parecer:** 1.469.151

**Apresentação do Projeto:**

Trata-se de uma solicitação de emenda ao projeto de pesquisa previamente aprovado pelo CEP em seres humanos desta instituição. A justificativa apresentada pelos pesquisadores responsáveis foram que após discussões do grupo de pesquisa, sugestões de membros da banca de qualificação do projeto e de colaboradores do projeto, foi considerado que a avaliação do efeito da crioterapia comparada a aplicação do placebo, ambos aplicados à mesma amostra de indivíduos hemiparéticos, proporcionaria
maior embasamento para esclarecer os questionamentos do estudo. Sendo assim trata-se de um estudo do tipo cross-over placebo-controlado, onde dezoito sujeitos
hemiparéticos crônicos participarão do estudo. A crioterapia será aplicada na região posterior da perna, na modalidade de pacote de gelo picado,durante 20 minutos. Inicialmente será aplicada a Escala de Escala Fugl Meyer.

**Objetivo da Pesquisa:**

O objetivo do presente projeto será avaliar os efeitos imediatos da crioterapia (pacote de gelo) sobre o desempenho neuromuscular, a propriocepção e a resistência passiva dos músculos dorsiflexores e flexores plantares do tornozelo, bem como sobre o desempenho na marcha em indivíduos hemiparéticos crônicos.

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**Avaliação dos Riscos e Benefícios:**

Em relação aos riscos o pesquisador responsável descreve que "o estudo está firmado nas condições de que oferece baixo risco à saúde do participante. Durante a aplicação da crioterapia é possível que haja uma sensação de desconforto pela diminuição da temperatura local. Após a realização dos testes de força é possível que haja sensação de desconforto pelo esforço. Vale destacar que a equipe envolvida no estudo prestará qualquer apoio necessário e que os profissionais envolvidos nas avaliações e intervenções são capacitados para tais. Os sujeitos serão cuidadosamente monitorados quanto à freqüência cardíaca e a pressão arterial. Caso algum procedimento promova dor ou desestabilização dos sinais vitais (hipertensão arterial e batimentos cardíacos) o mesmo será interrompido. Se necessário será encaminhado para uma unidade de saúde mais próxima. Também será feito o controle da temperatura da pele do
sujeito. Serão usados critérios para excluir qualquer indivíduo que possua complicações em decorrência da aplicação de frio, minimizando riscos.

Apenas fisioterapeutas aplicarão as compressas frias. Controle rigoroso da temperatura da pele será realizado, com um termômetro infravermelho.Qualquer desconforto anormal do que o esperado com as aplicações de gelo, se relatado, abortará o procedimento e aquecimento gradual será realizado na perna do sujeito.

O presente estudo traz benefícios como sua contribuição para a comunidade científica e clínica, auxiliando na reabilitação de sujeitos após um acidente vascular cerebral. Trará subsídios científicos para o entendimento da efetividade e dos mecanismos de ação da crioterapia (aplicação de pacote de gelo) nos membros inferiores de indivíduos hemiparéticos crônicos, embasando sua recomendação nos programas de reabilitação neurológica. Além disso, estudos neste âmbito são relevantes, tendo em vista que a crioterapia é um recurso de fácil aplicação, baixo custo,podendo ser aplicado na prática clínica ou no próprio ambiente domiciliar. Este estudo possibilita ainda o acesso à avaliação minuciosa e de alta
tecnologia. Será oferecido material educativo com objetivo de promover alterações na qualidade de vida através de incentivo à prevenção do AVC ou da reincidência do mesmo. Serão oferecidas orientações referentes ao cuidado do paciente neurológico.

**Comentários e Considerações sobre a Pesquisa:**

O projeto de pesquisa possui relevância à área em questão.





**Considerações sobre os Termos de apresentação obrigatória:**

Folha de rosto assinada e datada de acordo com as normas.O TCLE está de acordo com à Resolução nº466/2012.

**Recomendações:**

Nada a declarar.

**Conclusões ou Pendências e Lista de Inadequações:**

Projeto Aprovado.

**Considerações Finais a critério do CEP:**

O Comitê de Ética em Pesquisa (CEP) em seres humanos recomenda que os pesquisadores responsáveis consultem as normas do CEP e a resolução nº 466/2012, disponíveis da página da Plataforma Brasil em Caso de dúvidas.

**Este parecer foi elaborado baseado nos documentos abaixo relacionados:**

| Tipo Documento | Arquivo | Postagem | Autor | Situação |
|---|---|---|---|---|
| Informações Básicas do Projeto | PB_INFORMAÇÕES_BÁSICAS_517253 E1.pdf | 02/03/2016 15:41:21 | | Aceito |
| Folha de Rosto | folhaDeRosto_assinada.pdf | 02/03/2016 15:32:24 | Carolina Carmona de Alcântara | Aceito |
| Projeto Detalhado / Brochura Investigador | PROJETO_DOUTORADO_emenda.pdf | 02/03/2016 12:04:54 | Carolina Carmona de Alcântara | Aceito |
| Informações Básicas do Projeto | PB_INFORMAÇÕES_BÁSICAS_DO_P ROJETO_294488.pdf | 23/04/2014 09:48:45 | | Aceito |
| TCLE / Termos de Assentimento / Justificativa de Ausência | Termo de Consentimento Livre e Esclarecido.pdf | 23/04/2014 09:45:47 | | Aceito |

**Situação do Parecer:**
Aprovado

**Necessita Apreciação da CONEP:**
Não

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SAO CARLOS, 24 de Março de 2016

**Assinado por:**
**Ricardo Carneiro Borra**
**(Coordenador)**

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**Anexo II**

Universidade Federal de São Carlos
Centro de Ciências Biológicas e da Saúde – CCBS
Departamento de Fisioterapia

**TERMO DE CONSETIMENTO LIVRE E ESCLARECIDO**

1. Você está sendo convidado para participar da pesquisa: "EFEITOS IMEDIATOS DA CRIOTERAPIA SOBRE O DESEMPENHO NEUROMUSCULAR DA ARTICULAÇÃO DO TORNOZELO E O PADRÃO DA MARCHA DE INDIVÍDUOS HEMIPARÉTICOS ESPÁSTICOS CRÔNICOS PÓS-AVC".
2. Você foi selecionado por meio da lista de inscrição da Unidade Saúde Escola da Universidade Federal de São Carlos ou da comunidade local e sua participação não é obrigatória.
3. O objetivo deste estudo é avaliar os efeitos imediatos da crioterapia (pacote de gelo) sobre o desempenho neuromuscular e a resistência passiva dos músculos dorsiflexores e flexores plantares do tornozelo, bem como sobre o desempenho na marcha em indivíduos hemiparéticos crônicos e em indivíduos saudáveis.
4. Sua participação nesta pesquisa consistirá em: 1) Avaliação inicial por meio de uma ficha aplicada por um fisioterapeuta capacitado; 2) Avaliação da função do seu membro inferior por meio de escalas de funcionalidade; 3) Avaliação da cinemática da marcha; 4) Realização de testes em Dinamômetro Isocinético, concomitantemente à eletromiografia, para os movimentos do tornozelo; 5) Aplicação de pacote de gelo na região posterior da perna.
5. Este estudo está firmado nas condições de que oferece baixo risco à saúde do participante. Durante a aplicação da crioterapia é possível que haja uma sensação de desconforto pela diminuição da temperatura local. Após a realização dos testes de força é possível que haja sensação de desconforto pelo esforço. Vale destacar que a equipe envolvida no estudo prestará qualquer apoio necessário e que os profissionais envolvidos nas avaliações e intervenções são capacitados para tais.
6. Por outro lado, o presente estudo traz benefícios como sua contribuição para a comunidade científica e clínica, auxiliando na reabilitação de sujeitos após um acidente vascular cerebral. Trará subsídios científicos para o entendimento da efetividade e dos mecanismos de ação da crioterapia (aplicação de pacote de gelo) nos membros inferiores de indivíduos hemiparéticos crônicos, embasando sua recomendação nos programas de reabilitação neurológica. Além disso, estudos neste âmbito são relevantes, tendo em vista que a crioterapia é um recurso de fácil aplicação, baixo custo, podendo ser aplicado na prática clínica ou no próprio ambiente domiciliar. Este estudo possibilita ainda o acesso à avaliação minuciosa e de alta tecnologia. Será oferecido material educativo com objetivo de promover alterações na qualidade de vida através de incentivo à prevenção do AVC ou da reincidência do mesmo. Serão oferecidas orientações referentes ao cuidado do paciente neurológico.
7. O protocolo de avaliação da marcha e em dinamômetro isocinético, bem como a aplicação

da crioterapia não poderão ser realizados se o indivíduo apresentar Diabetes Mellitus; reações adversas ao frio; intolerância à aplicação do gelo; ausência de sensibilidade ao frio; presença do Fenômeno de Raynaud; úlceras ou lesões dermatológicas; doenças vasculares periféricas ou cardiovasculares graves (insuficiência cardíaca, arritmias ou angina pectoris); outras doenças ortopédicas ou neurológicas que comprometam coleta de dados; aplicação de toxina botulínica no período de até quatro meses antes do estudo; deficiências cognitivas ou de comunicação que impossibilitem a realização dos procedimentos; antecedentes de lesões articulares ou musculares nos membros inferiores; dor durante os procedimentos de avaliação; índice de massa corporal (IMC) maior que 28 kg/m².

8. Você será cuidadosamente monitorado quanto à freqüência cardíaca e a pressão arterial. Caso algum procedimento promova dor ou desestabilização dos sinais vitais (hipertensão arterial e batimentos cardíacos) o mesmo será interrompido. Se necessário será encaminhado para uma unidade de saúde mais próxima.
9. Não há métodos alternativos envolvidos nesse estudo.
10. A pesquisa será realizada por fisioterapeutas formados, experientes e capacitados. Quaisquer dúvidas que você tenha, você poderá acessar os dados da pesquisa e dos pesquisadores com os próprios pesquisadores, cujos contatos estão ao final deste documento e também no comitê de ética em pesquisa em seres humanos desta instituição.
11. Você será esclarecido sobre todos os procedimentos envolvidos na sua participação no estudo, antes e durante o curso da pesquisa. Você também será esclarecido quanto a sua participação no grupo de sujeitos que tiveram AVC (“derrame”) ou no grupo controle (para os que não tiveram AVC).
12. Você tem a liberdade em se recusar a participar ou retirar seu consentimento, em qualquer fase da pesquisa, sem penalização alguma e sem prejuízo ao seu cuidado.
    a. “A qualquer momento você pode desistir de participar e retirar seu consentimento.”
    b. “Sua recusa não trará nenhum prejuízo em sua relação com o pesquisador ou com a instituição.”
13. Garantimos o sigilo que assegure a sua privacidade quanto aos dados envolvidos na pesquisa. Todos os dados da pesquisa serão acessíveis apenas para os pesquisadores colaboradores do estudo. A divulgação na comunidade científica será realizada de forma que não seja divulgada a identidade dos participantes.
    a. “As informações obtidas através dessa pesquisa serão confidencias e asseguramos o sigilo sobre sua participação.”
    b. “Os dados não serão divulgados de forma a possibilitar sua identificação.”
14. Não haverá quaisquer gastos dos sujeitos do estudo com esta pesquisa.
15. Você receberá uma cópia deste termo onde consta o telefone e o endereço do pesquisador principal, podendo tirar suas dúvidas sobre o projeto e sua participação, agora ou a qualquer momento.

Carolina Carmona de Alcântara
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Rodovia Washington Luís, km 235, Monjolinho, São Carlos, SP, CP:13.565-905
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**Pesquisadores responsáveis: Prof. Thiago Luiz Russo e Ms. Carolina Carmona de Alcântara**

***Declaro que entendi os objetivos, riscos e benefícios de minha participação na pesquisa e concordo em participar.***

***O pesquisador me informou que o projeto foi aprovado pelo Comitê de Ética em Pesquisa em Seres Humanos da UFSCar que funciona na Pró-Reitoria de Pesquisa da Universidade Federal de São Carlos, localizada na Rodovia Washington Luiz, Km. 235 - Caixa Postal 676 - CEP 13.565-905 - São Carlos - SP – Brasil. Fone (16) 3351-8028. Endereço eletrônico:*** *cephumanos@power.ufscar.br*

São Carlos,____de______________de 20___.

_________________________________________
Nome e assinatura do sujeito da pesquisa

**Anexo III**

OXFORD
UNIVERSITY PRESS
Physical Therapy
Journal of the American Physical Therapy Association

# Cryotherapy reduces muscles spasticity, but does not improve post-stroke gait kinematics: a randomized controlled crossover study



| | |
|---|---|
| Journal: | *Physical Therapy* |
| Manuscript ID | PTJ-2017-0661 |
| Manuscript Category: | Original Research - Clinical Trial |
| Section: | Neurology |
| Keywords: | Muscle Tonus, Walking, Cryotherapy, Cerebrovascular Accident, Stroke |
| | |

# Anexo IV

Journal of Neurologic Physical Therapy

## Cryotherapy does not affect lower limb strength post-stroke: a randomized controlled study

--Manuscript Draft--

| | |
|---|---|
| **Manuscript Number:** | JNPT-D-17-00197 |
| **Full Title:** | Cryotherapy does not affect lower limb strength post-stroke: a randomized controlled study |
| **Article Type:** | Research Articles |
| **Corresponding Author:** | Thiago Luiz Russo, Ph.D.<br>Universidade Federal de Sao Carlos<br>São Carlos, São Paulo BRAZIL |
| **Corresponding Author E-Mail:** | thiagoluizrusso@gmail.com |
| **Manuscript Region of Origin:** | BRAZIL |
| **Abstract:** | Background and Purpose: Cryotherapy is among the techniques applied to spastic muscles in neurological patients in order to temporarily reduce spasticity, aiming at facilitating muscle performance and ultimately functional training, such as walking. However, its effects on muscle capacity to generate strength have not been studied in subjects post-stroke. Thus, the aim of this study is to investigate the immediate effects of cryotherapy (ice pack modality), applied to spastic plantarflexors muscles of subjects post-stroke, on isometric, concentric and eccentric torque of plantarflexors and dorsiflexors. Methods: This is a randomized controlled crossover study. Sixteen chronic hemiparetic subjects participated in this study. Cryotherapy (ice pack) or Control (room temperature sand pack) were applied to the calf muscles of the paretic limb. Torque assessments were performed using an isokinetic dynamometer, before and immediately after intervention. Results and Discussion: Cryotherapy application did not change the isometric, concentric and eccentric response compared to control application. These findings contribute to the evidence-based approach in the clinical rehabilitation post-stroke. If the goal is to increase muscle capacity to generate force in the lower limbs post-stroke, cryotherapy (ice pack modality) seems to not be effective. On the other hand, it is important to highlight that cryotherapy did not decrease the capacity to generate force as well, and most likely would not negatively affect functionality post- application. Conclusions: The findings of this study suggest that cryotherapy (ice pack) applied to the calf muscles of subjects with chronic hemiparesis does not affect dorsiflexion or plantarflexion strength. |
| **Keywords:** | Muscle Strength; Torque; Spasticity; Cold therapy; Stroke |

# Anexo V

**Neurorehabilitation & Neural Repair**

Neurorehabilitation &
Neural Repair

## Different Error Size During Locomotor Adaptation Affects Transfer To Over Ground Walking Post-Stroke

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|---|---|
| Journal: | *Neurorehabilitation and Neural Repair* |
| Manuscript ID | NNR-17-0368 |
| Manuscript Type: | Original Research Article |
| Date Submitted by the Author: | 07-Nov-2017 |
| Complete List of Authors: | Alcantara, Carolina; Federal University of Sao Carlos (UFSCar), Department of Physical Therapy<br>Charalambous, Charalambos; University of Delaware, Department of Physical Therapy<br>Morton, Susanne; University of Delaware, Department of Physical Therapy<br>Russo, Thiago; Federal University of Sao Carlos (UFSCar), Department of Physical Therapy<br>Reisman, Darcy; University of Delaware, Department of Physical Therapy |
| Keyword: | Stroke, Locomotion, Rehabilitation, Motor Learning |
| Abstract: | Background: Studies in neurologically intact subjects suggest that the gradual presentation of small perturbations (errors) during learning results in better transfer of a newly learned walking pattern to over ground walking. Whether the same result would be true after stroke is not known. Objective: To determine whether introducing perturbations gradually or abruptly during locomotor learning using a split-belt treadmill influences learning the novel walking pattern or transfer to over ground walking post-stroke. Methods: Twenty-six chronic stroke survivors participated and completed the following walking testing paradigm: Baseline overground walking; Baseline treadmill walking; Split-belt treadmill/Adaptation period (belts moving at different speeds); Catch trial (belts at same speed); Post overground walking. Subjects were randomly assigned to the Gradual group (gradual changes in treadmill belts speed during Adaptation) or the Abrupt group (a single, large, abrupt change during Adaptation). Step length asymmetry adaptation response on the treadmill and transfer of learning to over ground walking were assessed. Results: Step length asymmetry during the Catch trial was the same between groups (p=0.195) confirming that both groups learned a similar amount. The magnitude of transfer to over ground walking was greater in Gradual than Abrupt group (p=0.041). Conclusions: The introduction of gradual perturbations (small errors), compared to abrupt (larger errors), during a locomotor adaptation task seems to improve transfer of the newly learned walking pattern to over ground walking post-stroke. However, given the limited magnitude of transfer, future studies should examine other factors that could impact locomotor learning and transfer post-stroke. |
| | |