# Exploring the Efficacy of Using Ischemic Preconditioning (IPC) to Improve Neural Recruitment During Resistance Exercise After Spinal Cord Injury (SCI).

by

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ABSTRACT

The relationship between ischemic preconditioning and performance measures in able-bodied athletic populations have been thoroughly studied within the literature and demonstrated significant performance improvements. However, there is currently only one human study investigating how IPC can impact performance measures in individuals with a spinal cord injury (SCI). The mechanism that influences these performance improvements is still not fully understood. The purpose of this study was to investigate the effects of IPC in this population on performance measures, muscular force, and neural contribution. This study utilized 4 participants who have experienced a SCI. The study design was a repeated-measures, cross-over model. It consisted of an IPC (220mmHg) and SHAM (20mmHg) condition in random order. Functional measures of skeletal muscle force and neural measures with surface electromyography were recorded. The performance measures were maximum voluntary contractions (MVC) of the forearm muscles and a time to task failure (TTF) handgrip test. Results: IPC did not improve performance output between both conditions in a TTF handgrip test (IPC: 25.295±10.371 mins; SHAM: 20.958±7.621 mins). IPC did not improve muscular force recorded as MVC (IPC: 571.38 241.83 N; SHAM: 543.32±210.89 N). IPC did not improve neural recruitment suggested in root mean square (RMS) values during the TTF handgrip test in both measured muscles, the flexor carpi radialis (FCR) and the flexor carpi ulnaris (FCU), (FCR RMS: $p = 0.564$; FCU RMS: $p = 0.863$). More data is need for statistical relevance and to determine if there is a relationship between IPC and performance in individuals who have experienced a SCI, and if neural contribution plays a role.

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# CHAPTER 1

# INTRODUCTION

## General Introduction

Ischemic Preconditioning (IPC) was first utilized in the clinical setting and has shown to promote cardioprotective effects in both animal and human models. The technique was originally a surgical procedure where application of occlusion was placed directly on the coronary artery of the heart. This created an ischemic environment and the body's stress response led to lasting cardioprotection (Murry et al., 1986; Przyklenk et al., 1993). Over time, IPC evolved into a remote application which has been shown to improve both cardiac and skeletal muscle function (Hausenloy & Yellon, 2008; Kharbanda et al., 2009; Lamidi et al., 2021; Lang & Kim, 2022). This intervention today most commonly follows the noninvasive application of a cuff, similar to a blood pressure cuff, wrapped around the superior portion of a limb, and alternates between cycles of full occlusion and reperfusion. The number of cycles and duration varies upon studies. Additionally, IPC has been utilized in exercise performance protocols and has been shown to improve performance measures in various settings. Studies have looked at the impact of this intervention on many different measures ranging from single limb isometric maximal contractions (Barbosa et al., 2015; Halley et al., 2018; Telles et al., 2022) to maximal power output performance measures of cycling (Crisafulli 2011; Cruz et al., 2015; Paradis-Deschênes et al., 2020), kayaking (Halley et al., 2020), swimming (Jean St-Michel et al., 2011), sprinting (Griffin et al., 2019; Paradis-Deschênes et al., 2020), basketball (Cheng et al., 2021), and rhythmic handgrip (Barbosa et al., 2015). In sports performance literature focusing on athletes, IPC has been shown to improve performance and fatigue measures (Barbosa et al., 2015; Cheng et al., 2021; Crisafulli 2011; Cruz et al., 2015; Griffin et al., 2019; Halley et al., 2020; Paradis-Deschênes et al., 2020; Jean St-Michel et al., 2011).

The mechanisms behind the reported benefits of IPC are not fully understood. Previous research suggests findings linking to humoral, metabolic, and neural pathways. Specifically, the most commonly suggested mechanisms leading to the improvements in performance appear to be increased oxygen and blood flow to the muscle engaged in action (Andreas et al., 2011; Barbosa et al., 2015; Cheng et al., 2021; Griffin et al., 2019; Kimura et al., 2007; Paradis-Deschênes et al., 2020; Patterson et al., 2015; Tomschi et al., 2018). Many studies have provided hypotheses regarding why performance increases, but more specific findings are needed to fully determine the driving forces behind the benefits of this intervention. This study is testing out the hypothesis that there is an influence of neural drive causing the improvements in performance measures.

The neural pathway is one of the least explored contributing factors, with only a few studies investigating this possible mechanistic pathway. Early findings from an animal study suggests that IPC increases neural feedback by demonstrating more motor recruitment in the working skeletal muscle supported by larger EMG potentials, which represents total motor neural activity, after IPC intervention (Phillips et al., 1997). It wasn't until recently, however, that study results from athletic able-bodied populations speculated a possible neural benefit. The findings displayed a delay in onset of fatigue and better performance measures after IPC (Barbosa et al., 2015; Cruz et al., 2016). These results were supported by a higher EMG potential (Cruz et al., 2016) and an increase in the rate of force development for the given task ((Barbosa et al., 2015). This data provided early evidence of increased neural drive from IPC in humans (Barbosa et al., 2015; Cruz et al., 2016).

A majority of research investigating neural facilitation following IPC has focused on able-bodied populations, however individuals with neural impairments may also benefit from this intervention. Out of the limited number of studies, IPC has demonstrated an increase in performance output in individuals with an impairment relating to the central nervous system (CNS) (Chotiyarnwong et al., 2020; Hyngstrom et al., 2018; Seeger et al., 2015). For individuals with Multiple Sclerosis (MS), IPC before a six-minute walk test increased the distance walked by 5.7%. In addition, maximal knee extensor strength was increased by an average of 16% in individuals who have experienced a stroke after IPC intervention on their more affected leg. This improvement was accompanied by an increase in EMG potentials by an average of 31% (Hyngstrom et al., 2018). One population that may also benefit from IPC are individuals who have experienced a spinal cord injury (SCI). To the writer's knowledge, only a single study has investigated the effects of IPC on individuals who have experienced a SCI at this time. The study focuses on aerobic performance measures and these authors observed an improvement in maximal arm crank test performance by an average of 4%. Mechanistic contributing factors were not measured in this study (Seeger et al., 2015). It is plausible that improvements in performance were related to improved neural recruitment, however this has yet to be determined.

**Purpose of Study**

The purpose of this study is to investigate whether or not neural recruitment, measured via surface electromyography (sEMG), is acutely improved after ischemic preconditioning in individuals with spinal cord injury. A secondary aim is to determine whether hand-grip strength in this population is improved after ischemic preconditioning, in a constant load rhythmic handgrip protocol until failure, and if so, whether these improvements are related to improved neural recruitment.

# CHAPTER 2

# LITERATURE REVIEW

## Background of IPC in Cardiac Setting

The intervention of ischemic preconditioning (IPC) was first utilized in the clinical setting with animal models and has shown to promote cardioprotection (Murry et al., 1986; Przyklenk et al., 1993). It began as an invasive technique where clamping was placed directly on the focal area, starting with the heart, and induced occlusion. This evoked an ischemic response. In these early studies, injury and intervention stimuli were performed specifically on the coronary artery and it was demonstrated that the infarct size and damage was decreased by 25-35% in the animals receiving intervention (Gho et al., 1996; Murry et al., 1986; Przyklenk et al., 1993). Occlusion was then applied to other organs and displayed reciprocal results to the direct application (Kharbanda et al., 2009). In summary, promising cardioprotective effects were shown by decreasing ischemic injury and improving recovery from infarct (Deferrari et al., 2017, Gho et al., 1996; Murray et al., 1986; Przyklenk 1993). After these initial studies, it was trialed out on more accessible locations such as the arms and legs in both human and animal models (Hausenloy & Yellon, 2008; Lang & Kim 2022; Lamidi et al., 2021).

The transition from animal models to human subjects initially led to some inconsistencies

due to the limitation of control in both the subjects and intervention specifics. In time, the majority of human studies investigating these factors found the same positive improvements regarding the cardiovascular system (Deferrari et al., 2017; Lang & Kim, 2022). The application of this intervention has demonstrated resistance to damage and improved functioning both before and after an injury on the heart, other organs, and muscles (Defarrari et al., 2017; Khabanda et al., 2009; Lamidi et al., 2021; Lang & Kim, 2022; Sharma et al., 2015). These discoveries led to the consideration that IPC could be utilized in other settings for different benefits such as exercise and performance.

## Intervention Transition to Exercise Performance

As the positive effects from IPC advanced in the clinical setting, it brought attention to the relationship between IPC and skeletal muscle, specifically on how it could improve exercise performance measures (Crisafulli et al., 2011; Sharma et al., 2015). It was speculated that the protective measures from this intervention could decrease the amount of stress induced on a muscle, allowing better performance output.

As a point of clarification, there are several different terms used to define the intervention in this setting as it has evolved over time. Some of these terms are remote ischemic preconditioning (RIPC), local ischemic preconditioning (LIPC), and ischemic preconditioning (IPC). For the purpose of this thesis, IPC will be used as the broad term throughout. The application of IPC and how it is more appropriately utilized today, in human subjects, focused on muscular response, is similar among studies. IPC is an intervention where a cuff is placed around a limb and can range from one to all four limbs. It alternates through cycles of full occlusion to reperfusion for a period of time. The most frequently used protocol for exercise measures in human subjects is from the early introductory studies investigating IPC in animals (Caru et al., 2019; Lang & Kim, 2022; Murry et al., 1986; Przyklenk et al., 1993). This consists of alternating cycles of occlusion around 200-220 mmHg, and reperfusion, for either 3 or 4 cycles for 5 minutes.

Both of these protocols have shown favorable results in the literature (Arriel et al., 2020; Caru et al., 2019; Lang & Kim, 2022; Sharma et al., 2015).

However, a main factor that differs among studies is the specific cuff intervention time and duration of cycles in their protocol. Due to these differences, this is the most common variance when comparing studies and validity of results. When looking into this further, it has been demonstrated that the amount of IPC exposure has a positive correlated response on the protective impact in the clinical setting (Lamidi et al., 2021; Lang & Kim 2022; Loukogeorgakis et al., 2007). This benefit translates to having an impact on performance increase based on the amount of muscle (or tissue) mass exposed as well as the duration of the intervention (Barbosa et al., 2014; Lamidi et al., 2021). More research needs to be done to determine which cuff intervention is most advantageous for each of the populations studied.

## **IPC Improving Exercise Performance in Able-bodied Population**

When looking at the efficacy of IPC across studies over time, with able-bodied and the athletic population, it has been demonstrated to show improvements in performance measures being tested. Given the complexity of these measurements, IPC has been shown to enhance performance in a variety of athletic settings and measures ranging from aerobic to anaerobic tasks. When comparing the effects to a placebo in broad performance measures in subjects with varying exercise levels, studies have demonstrated a range of 2-11% in overall improvements (Barbosa et al., 2014; Cheng et al., 2021; Crisafilli 2011; Cruz et al., 2015; Cruz et al., 2016; Griffin et al., 2019; Halley et al., 2020; Jean St-Michel et al., 2011; Paradis-Deschênes et al., 2020; Patterson et al., 2015; Tomschi et al., 2018). Although benefits are seen throughout a variety of training modalities, the most advantageous change may be in aerobic and high intensity types of training (Halley et al., 2019; Salvador et al., 2016). Aerobic improvement has been demonstrated in cycling, swimming, running, rowing, and handgrip exercises.

To begin, when narrowing in specifically on the elite athletic population subjects and the effects of IPC, there is a decrease in the amount of improvement seen with a range of 1-4% increase in overall performance (Cheng et al., 2021; Halley at al., 2020; Jean St-Michel et al., 2011; Paradis-Deschênes et al., 2020). As suggested above, it is possible that more improvement could be seen if this specific elite athletic population had longer intervention exposure. Additionally, with this athletic population, the trained individuals are often thought to be performing at peak levels as their baseline values due to specific adaptations for their sport. Being able to decrease the time it takes to finish a task or improve performance output even minimally still makes an impactful effect on performance at this level of competition. It has been suggested that an elite performer increasing abilities by 0.4% is considered a competitively significant increase (Jean St-Michel et al., 2011).

In addition, numerous studies focused on how IPC can positively affect fatigue. It has been demonstrated multiple times that IPC delays the onset of fatigue and allows subjects to work more efficiently (Barbosa et al., 2015; Cheng et al., 2021; Crisafulli 2011; Halley et al., 2020; Jean St-Michel et al., 2011; Patterson et al., 2015; Tomschi et al., 2018). IPC before a variety of different performance measures has also shown to increase maximum performance output (Barbosa et al., 2015; Cheng et al., 2021; Crisafulli 2011; Jean St-Michel et al., 2011). It is also relevant to address the post exercise effects of IPC in able-bodied and athletic populations because oftentimes there is not appropriate rest between exercise, practices, and events. A recent meta-analysis has demonstrated that a majority of studies, investigating how IPC affects the stress impact on muscle after exercise, displayed some form of muscular repair and better performance afterwards (Arriel et al., 2020). The common unknown is the underlying mechanism that leads to the benefit seen in performance measures.

Lastly, there are some inconsistencies when comparing IPC studies due to the many varying factors ranging from intervention protocol to subject demographics. As addressed above, the cuff intervention specifics vary, and is one of the main contributors to the differing results (Lamidi et al., 2021; Salvador et al., 2016). Although there is a protocol that is predominantly used from some of the original studies, there is not a universal testing protocol. A recent study investigated the relationship between intervention protocol specifics and fitness level and determined that they have an impactful relationship. Both training level and amount of intervention exposure have demonstrated different effects on individuals. It is suggested that in order for well-trained athletes to get more promising benefits, they will need more exposure compared to average trained individuals (Arriel et al., 2020; Barbosa et al., 2014). This finding indicates that there may not be a one size fits all approach for this intervention in each differing population (i.e. endurance athletes, sprint athletes, level of competition, etc.).

## Proposed Mechanism of Action

There has been a decade of investigation exploring the efficacy and mechanism behind IPC and the effects on exercise performance. Various studies have demonstrated that IPC delays the onset of fatigue in many different exercise measures such as maximal voluntary contractions, short-term exercise performance, repeated measures in performance, and time to exhaustion tasks. Additionally, IPC has been shown to increase maximal performance output while performing at a more efficient rate (Barbosa et al., 2015; Cheng et al., 2021; Crisafulli 2011; Halley et al., 2020; Jean St-Michel et al., 2011; Patterson et al., 2015; Tomschi et al., 2018). As a whole, the majority of research studies have indicated that IPC leads to improvements, but the exact mechanism is still not understood. The general contributing factors to these achieved benefits are thought to be humoral, metabolic, and neural pathways.

To start, the most commonly found mechanisms supporting these enhancements are that IPC leads to an increase of cardioprotective factors (Jean St-Michel et al., 2011; Khabanda et al., 2009; Lamidi et al., 2021; Lang & Kim, 2022), greater oxygen uptake and increased blood flow in the working skeletal muscle (Andreas et al., 2011; Barbosa et al., 2015; Cheng et al., 2021; Griffin et al., 2019; Kimura et al., 2007; Paradis-Deschênes et al., 2020; Patterson et al., 2015; Tomschi et al., 2018), and more adapted metabolic pathways (Andreas et al., 2011;Cheng et al., 2021; Griffin et al., 2019; Jean St-Michel et al., 2011). It is thought that the efficiency in work is due to a decrease in oxidative stress (Halley et al., 2020; Tomschi et al., 2018), increased ATP preservation and availability (Andreas et al., 2011; Cheng et al., 2021; Griffin et al., 2019; Jean St-Michel et al., 2011), and increased RBC deformability (Tomschi et al., 2018). With the current findings, it is possible that there is not one exact mechanism contributing to the beneficial but complex adaptations, and that it is a combination of humeral, metabolic, and neural pathways.

Currently, the research is lacking on the possible neural influence from IPC. Only a few human studies have looked into the neural effects contributing to the improvements in exercise performance after IPC. In aerobic exercise testing for healthy individuals, the acute benefits demonstrated higher EMG potentials and muscle activation (Cruz et al., 2016) as well as a significant increase in rate of force development (Barbosa et al., 2015). The reasoning behind these improvements was thought to be driven by an increase in voluntary neural drive (Barbosa et al., 2015, Cruz et al., 2016). These studies have set a foundation for further understanding on the possible connection between IPC and neural drive, however, are not without limitations. First, the study using cyclist athletes only took EMG signal measurements on a single leg and single muscle, being the right vastus lateralis. Cycling engages multiple quadricep muscles, therefore, it could possibly give more promising data to support the contribution of the neural recruitment if signals were recorded on both legs and in multiple locations for better activation outcome measures (Pietrosimone et al., 2011). Additionally, both studies utilized athletes and had a small sample size. A larger subject group supplying more data could lead to more reliable results. Furthermore, previous data demonstrated healthy individuals received more benefit from IPC in performance measures compared to athletes (Arriel et al., 2020). It is possible that trialing out different populations could potentially lead to a greater increase in neural drive compared to athletic able-bodied subjects.

**IPC Improving Exercise Performance in Different Populations**

Although IPC started in the clinical setting with cardiac patients, it is now primarily studied in athletics to improve exercise performance. There are similar findings throughout the effectiveness of IPC that an individual's fitness level and health status play a role in the amount of benefit obtained (Barbosa et al., 2014; Lamidi et al., 2021; Loukogeorgakis et al., 2007). When comparing the results in exercise performance from healthy non-athletes to elite athletes, there was a greater improvement in the healthy non-athletes (Arriel et al., 2020). Additionally, IPC after exercise demonstrated a decrease in exercise induces stress and increased exercise capability (Paradis-Deschênes et al., 2020). These findings suggest that IPC could possibly aid in restoring skeletal muscle after damage. Based on the effects it has on performance, delaying fatigue, and recovery after exercise, it is possible IPC can further benefit different types of athletes such as individuals with impairments, specifically ones with compromised neurological functioning.

The efficacy of IPC and the mechanism behind it, with a focus on health complications or injuries that affect the central nervous system (CNS), has not been thoroughly studied. There are a few studies, however, that demonstrate these relationships. For specific conditions such as Multiple Sclerosis, Stroke, and Spinal Cord Injury, IPC has demonstrated a beneficial effect in the investigated performance measures. In general, studies looking at individuals with an impairment relating to the CNS and exercise performance, IPC led to an increased range of 4-16% in performance measures (Chotiyarnwong et al., 2020, Hyngstrom et al., 2018, Seeger et al., 2015). In comparison, previous studies demonstrated a performance improvement range of 1.11-4% specifically only in elite athletic able-bodied individuals (Cheng et al., 2021; Halley at al., 2020; Jean St-Michel et al., 2011; Paradis-Deschênes et al., 2020). In subjects with varying exercise levels, not solely elite athletes, a range of 2-11.2% in overall improvement was indicated (Barbosa et al., 2014; Cheng et al., 2021; Crisafilli 2011; Cruz et al., 2015; Cruz et al., 2016; Griffin et al., 2019; Halley et al., 2020; Jean St-Michel et al., 2011; Paradis-Deschênes et al., 2020; Patterson et al., 2015; Tomschi et al., 2018). From these findings, the largest increase in exercise performance values was seen in the least exercise adapted group. An even larger benefit was seen when including individuals with a form of impairment and their performance improvement values. These findings support that greater improvement from IPC is demonstrated in compromised populations.

A recent study with 75 participants diagnosed with MS demonstrated that IPC improved distance walked in a timed walking test by an average of 5.7% (Chotiyarnwong et al., 2020). Although mechanistic factors were not measured, the authors suggest these findings could be from IPC producing protective effects against atrophy and motor functioning degeneration (Chotiyarnwong et al., 2020). This suggestion is aligned with earlier studies that demonstrated IPC leading to protective effects on the cardiovascular system.

Furthermore, the effects of IPC on individuals who have experienced a stroke reveal an average increase of 16% in strength on the leg that was more affected from the stroke, the paretic leg (Hyngstrom et al., 2018). This study demonstrated a positive relationship between IPC and functionality. The more impaired limb received a significant benefit from the intervention. The mechanism behind these results were investigated and it was found that the participants had an average increase in EMG potential of 31%. The performance measure in this study was maximal contractions of the knee extensor. From previous data, IPC has indicated further and more consistent benefit on aerobic performance measures compared to anaerobic (Halley et al., 2019; Salvador et al., 2016**)**. Utilizing this different population with an aerobic based exercise task could lead to more reliable results. Despite the limitations, these findings support the idea that IPC may have an effect on neural activation and lead to an improvement in testing in someone with impaired neural functioning (Hyngstrom et al., 2018).

## IPC and Individuals with Spinal Cord Injury

IPC has demonstrated an increase in performance for elite athletic populations in the current literature, even though this specific population is thought to already be performing close to peak levels. In comparison, a majority of studies investigating IPC have demonstrated an even larger increase in performance for untrained able-bodied individuals. When comparing the benefit in untrained able-bodied individuals to the limited literature investigating individuals with a neurological impairment, the amount of improvement is increased. For individuals who have experienced a SCI, it is thought that they will experience greater benefit from IPC due to having neural limitations from the injury.

There is limited data out to identify the relationship and cause behind IPC on individuals with a spinal cord injury and performance measures. In a recent animal study investigating the neurological functioning of the limbs evaluating both motor and sensory performance after an induced SCI and IPC intervention, performance was improved by an average of 50% (Bashir et al., 2020). In addition, inflammatory and oxidative stress markers such as AOPP, TNF-, IL6, and PGE2, were significantly reduced in the animals that experienced the intervention compared to placebo or sham (Bashir et al., 2020). For human subjects with an SCI, IPC improved maximal performance on average by 4% (Seeger et al., 2015). More data is needed to determine if IPC benefits individuals with a SCI and the driving force behind the benefits. Since individuals with a SCI have compromised neural activity, it is possible that they may gain further benefits and demonstrate more recruitment activity leading to the mechanistic effect driven by neural activity.

## Aims and Hypothesis

The primary aim of this study was to investigate whether or not neural recruitment was acutely improved after ischemic preconditioning in individuals with spinal cord injury. It was hypothesized that neural recruitment, as defined by RMS amplitude, will increase after ischemic preconditioning during continuous, intermittent handgrip exercise to task failure in individuals with spinal cord injury as compared to a SHAM intervention.

The secondary aim was to determine whether acute, maximal effort handgrip strength in this population is improved after ischemic preconditioning. It was hypothesized that maximal effort handgrip strength, as defined by maximal voluntary contraction, will be improved after ischemic preconditioning in individuals with a spinal cord injury as compared to SHAM intervention.

# CHAPTER 3

# METHODS

This chapter describes the general procedures that were performed to determine participant eligibility and the study protocol sessions. For participants, inclusion and exclusion criteria is listed below. The consent process, three meeting times, the familiarization session, two experimental sessions, and data collection tools are described in detail. This study was approved by the ASU IRB.

## Study Overview

The study design was a repeated-measures, cross-over model with an intervention (IPC) and control (SHAM) condition. There was a consent process around 30 minutes, an initial familiarization session around 1 hour and two experimental conditions (IPC and SHAM) which required approximately 4 hours each to complete. The participant came to the lab on three occasions. The first was the consent and familiarization sessions. The second and third occasion will be the two experimental sessions. The total time commitment for the participant was estimated around 9.5 hours.

## Participants

Below is the inclusion criteria for this study:

- You have a spinal cord injury (SCI) and no recent history of autonomic dysreflexia
- No previous pathological condition that affects the lower limbs other than the SCI

- No contraindications to exercise as indicated by the Physical Activity Readiness Questionnaire (PAR-Q+) and the Exercise Preparticipation Health Screening Questionnaire for Exercise Professionals by the American College of Sports Medicine (ACSM)
- Not currently taking medicine or experiencing illness that may influence the neuromuscular system
- Age ≥18 and ≤ 55 years old and injury free (skeletal muscle) for > 3 months

The following special (vulnerable/protected) populations will be excluded:

- Minors (under 18)
- Adults who are unable to consent (impaired decision-making capacity)
- Prisoners
- Pregnant Women

For eligibility, a pre-screening communication session via zoom or in person was used to ensure the vulnerable/protected populations are not included in this study. The potential participants were pre-screened with the relevant tools (PAR-Q+, ACSM's Exercise Preparticipation Health Screening Questionnaire for Exercise Professionals, ASIA Impairment Scale) as recommended by the national governing body the American College of Sports Medicine (ACSM). Given the aims and the overall nature of the study design, there was a need to include the protected/vulnerable populations identified above.

**<u>Sample Size Estimate</u>**

The power analysis ran for this study indicated a sample size of 29 participants. This was based off of a projection of a large effect size and previous literature. The estimated effect size used was 0.7.

**Consent Process**

The consent process included a 30-minute introduction of the study procedures and requirements for participation as well as review of participant rights and resources for consent and the voluntary nature of study participation. Participants were informed of their right to refuse participation at any point, without suffering negative consequences and be provided with the contact information for the PI. Before participation, informed consent was obtained for each individual.

**Familiarization Session**

Once the participant was deemed eligible based off of the pre-screening, and informed consent was obtained, An ASU medical professional did a full evaluation including the International Standards for Neurological and Functional Classification of Spinal Cord Injury (ISNCSCI). Next, the general procedures of the experiment were explained, and the participant was introduced to the procedures involved in the study. The familiarization session included experiencing a 3-5 s handgrip maximal voluntary contraction (MVC) with both hands and the IPC protocol. Lastly, the pre-test guidelines were explained and given as a handout in regard to restriction of caffeine (12 hours), alcohol (24 hours), strenuous lower body exercise (48 hours) and instructions as to replication of food intake (24 hours) prior to the experimental trials.

**Experimental Sessions**

These sessions were a repeated-measures, cross-over design. It consisted of an IPC (occlusion pressure of 220mmHg) and SHAM (occlusion pressure of 20mmHg) condition in random order. It included functional measures of skeletal muscle force and neural measures with surface electromyography at baseline and 12 minutes after IPC or SHAM treatment. The two experimental sessions were separated by a minimum of 4 days and a maximum of 2 weeks.

Upon arrival at the laboratory, participants were fit for Surface EMG (sEMG) (refer to Neural Measures: Surface Electromyography (sEMG). They completed a standardized handgrip MVC warm-up (2 x 60% effort, 2 x 70% effort, 2 x 80%) with a handgrip dynamometer. Next, measurements of handgrip MVC were recorded. Thereafter, participants underwent either IPC or SHAM treatments depending on the trial. Occlusion alternated ensuring a total IPC or SHAM time of 60 min. The inflatable cuff (Personalized Tourniquet System; Owens Recovery Science, Delfi Medical Innovations, Vancouver, Canada) was positioned proximally on the arm above the elbow crease in a similar fashion as used to measure brachial artery blood pressure. On the nondominant arm, blood pressure measurements were recorded at the beginning of each 5 minute period, for a total of 12 times. To minimize any placebo effect, participants were told that the purpose of the study was to compare two different cuff pressures that could both improve exercise performance. Lastly, 12 minutes after the last cycle of reperfusion measurements of handgrip MVC and the TTF handgrip test were recorded.

Below is a representation of the experimental sessions protocol:

| **MVC warmup** (both arms) | **MVC baseline** (both arms) | **Cuff Intervention** 6 cycles alternating 5 mins of occlusion and reperfusion (dominant arm only) | **MVC post-intervention** (both arms) | **TTF Handgrip Test** (dominant arm only) | **MVC final** (both arms) |
|---|---|---|---|---|---|

**Ischemic Preconditioning (IPC)**

The IPC interventions was performed under ambient conditions with the participant in a seated position, and blood flow to the proximal (upper) dominant arm restricted via the inflation of a blood pressure cuff to either 220 mmHg (IPC) or 20 mmHg (SHAM) for six 5 min periods interspersed by a 5 min reperfusion. A Personalized Tourniquet System (PTS; Owens Recovery Science, Delfi Medical Innovations, Vancouver, Canada) was used to occlude the limb during both IPC and SHAM conditions. The PTS is specifically designed to safely regulate and control occlusion pressures. To minimize any placebo effect, participants were told that the purpose of the study was to compare two different cuff pressures that could both improve exercise performance.

**Performance Measures: TTF Handgrip Test**

Participants used a handgrip dynamometer (Biometrics Ltd G200) in a seated position with their arm at their side, elbow flexed at 90°, with the forearm in neutral positioning. They performed repetitive handgrip contractions in a rhythm of 60 contraction-relaxation cycles per minute guided by a metronome. On a large monitor, a visual aid was provided to show live contractions during this test. The participant was instructed to have the contractions stay within a scale that represented 40-45% of their MVC values. This test was completed when at least three contractions fell below the provided scale (contractions below 40% of their MVC). Participants were blinded to the duration, contraction force output, the range of the scale, and the failure criteria. Verbal encouragement was given along with correction to get back in rhythm with the metronome if needed. Time to task failure (TTF) was measured by the start being the first valid contraction and the end being the last valid contraction before failure.

**Muscular Force: Maximal Voluntary Contractions (MVCs)**

Arm MVC's were performed using a hand grip dynamometer measuring grip strength where participants are in a seated position with their arm at their side, elbow flexed at 90°, with the forearm in neutral positioning. Force signals were continuously sampled from both arms at 1000 Hz (Powerlab, ADInstruments, Sydney, Australia) and a 10 Hz low pass filter was applied. MVC measurements were recorded at three timepoints for both IPC and SHAM conditions. A minimum of three MVC's were recorded, or until at least three contractions ranged within 5% from each other with a one minute break for rest in between each MVC. Values were recorded at the start of the experimental session as a baseline after the intervention, and after both intervention and handgrip test were complete. The recorded MVC values were averaged.

**Neural Measures: Surface Electromyography (sEMG)**

Forearm surface EMG signals were recorded from both right and left flexor carpi radialis (FCR) and flexor carpi ulnaris (FCU) muscles using bipolar 10 mm Ag-AgCl surface electrodes during the MVCs and Handgrip test (ADInstruments Powerlab, Colorado Springs, CO). The electrodes were placed in bipolar configuration parallel to the direction of the muscle fibers according to standard recommendations (Hennessey, 1995) after careful skin preparation (shaving excess hair, careful abrasion with fine sandpaper and cleaning the skin with isopropyl alcohol swabs). The FCR electrode placement was around 3-4 fingerbreadths distal to the midpoint of a line connecting the medial epicondyle and biceps tendon. The FCU electrode placement was around 2 fingerbreadths volar to the ulna at the junction of the upper and middle thirds of the forearm (Hennessey, 1995). Placement was recorded for each participant to ensure consistency between sessions.

**Data Analysis**

Due to differing exercise durations between subjects and both IPC and SHAM conditions, the neural measures during the TTF handgrip test of the FCU and FCR RMS values were normalized and compared at 6 different timepoints being baseline (BL), 20%, 40%, 60%, 80%, and 100%, relative to TTF. Each timepoint value was calculated by locating the start of each (BL, 20%, 40%, 60%, 80%, and 100%) and calculating the average of the first 4 contractions at that specific point.

sEMG values were measured using the ML138 Dual BioAmp (common mode rejection ratio > 85 dB at 50 Hz, input impedance 200 MΩB) with 16-bit analog-to-digital conversion, sampled at 2000 Hz (ADInstruments, Sydney AUS). The recorded signals were filtered with a fourth-order Bessel filter between 20 and 500 Hz and smoothed for analysis with a root-mean-square calculation (RMS, 100 ms moving average window).

**Statistical Analysis**

Statistical analysis was completed using IBM SPSS Statistical version 28 (SPSS Inc., Chicago, IL). Data is presented as M ± SD. Analysis of the studentized residuals showed that there was normality, as assessed by the Shapiro-Wilk's test of normality on the studentized residuals ($p > 0.05$) for MVC and TTF. RMS FCR values were normally distributed ( $p > 0.05$) except for IPC BL (p=0.023), IPC 20% (p=0.007), IPC 40% (p=0.003), IPC 60% (p=0.002), IPC 80% (p=0.019), IPC 100% (p=0.004). RMS FCU values were normally distributed ( $p > 0.05$) except for SHAM BL (p=0.018), SHAM 40% (p=0.002) and given the low sample size this is understood. All data collected demonstrated no outliers, as assessed by no studentized residuals greater than ± 3 standard deviations. Differences in muscle force, neural recruitment (RMS) and muscle oxygenation were assessed using a RMANOVA (condition x time). Difference in performance (TTF) was assessed using a dependent T-test to determine whether there was a statistically significant mean difference between TTF when participants underwent IPC conditions to SHAM conditions. Significance was set at $p < 0.05$.

CHAPTER 4

# RESULTS

Due to data collection challenges, it is acknowledged that there are limitations to the analyses as a result of the low sample size. However, for the purpose of this thesis, all statistical procedures have been conducted as if the study was adequately powered. The data collection will continue beyond this thesis, and the following presentation should be viewed as pilot data.

## Performance Measures

There was no difference in performance time in the TTF handgrip test after the IPC condition (25.2950 ± 10.371), compared to the SHAM condition (20.958 ± 7.621). The difference between conditions was not significant (p=0.04).

## Muscular Force

Mean standard deviation of all MVC data is presented in table 1. There was no statistically significant two-way interaction between condition and time, $F(1, 2) = 1.29$, $p = 0.392$. The main effect of treatment showed no statistically significant difference in MVC values between trials, $F(1,2) = 42.44$, $p = 0.023$.The main effect of time showed that there was no statistically significant difference in MVC values between time points, $F(1,2) = 26.09$, $p = 0.036$.

**Neural Measures**

The RMS values of the flexor carpi radialis (FCR) muscle indicated that there was no statistically significant two-way interaction between condition and time, $F(5,15) = 0.625$, $p= 0.516$. The main effect of treatment showed no statistically significance in RMS FCR values between trials, $F(1,3) = 0.419$, $p=0. 564$. The main effect of time showed that there was no statistically significant difference in RMS FCR values between time points, $F(5,15) = 0.379$, $p = 0.673$.

The RMS values of the flexor carpi ulnaris (FCU) muscle indicated that there was no statistically significant two-way interaction between condition and time, $F(5,15) = 0.877$, $p= 0.520$.The main effect of treatment showed no statistically significance in RMS FCU values between trials, $F(1,3) = 0.035$, $p= 0.863$.The main effect of time showed that there was no statistically significance difference in RMS FCU values between time points, $F(5,15) = 0.388$, $p= 0.589$.

# CHAPTER 5

# DISCUSSION

This study experienced data collection challenges due to the COVID19 pandemic and limited availability to this specialized population. The recruitment period for this study began in March 2021 and is currently still working towards getting more individuals to participate. Connections were made with various adaptive sports facilities and locations with communities of individuals who have a form of impairment. This includes Ability360 Sports & Fitness Center, Arizona Disable Sports, ASU Sun Devils Adapt, ASU Accessibility Coalition, AZ Spinal Cord Injury Association, Kelly Brush Foundation, U of A Adaptive Sports Program, and local physical therapy and rehab clinics. Unfortunately, so far, only limited individuals were able to participate due to barriers of not meeting the criteria or not having the time. The current literature investigating IPC primarily utilizes more broad subject inclusion criteria making participant recruitment less limited and more attainable. Due to this, and as addressed at the beginning of the Results, discussion and critique have been provided with the understanding that the results may be different with a larger study population.

The purpose of this study was to determine if IPC led to performance improvements in MVC measures and a fatiguing task in individuals who have experienced a spinal cord injury, and if so, if those improvements were due to improved neural recruitment. Contrary to the hypothesis, the main outcome found was that IPC did not improve performance output. Time to failure of the handgrip test was not different after IPC (25.295 ± 10.371 min) compared to SHAM (20.958 ± 7.621) conditions (figure 1). Secondly, muscular force recorded as MVC values was not different in both pre and post measures in the study (table 1, figure 3). After intervention, values did not differ after IPC (571.38 ± 241.83) and SHAM (534.32 ± 210.89) conditions (table 1, figure 3). Lastly, there was no evidence to demonstrate improved neural recruitment after IPC condition compared to SHAM. FCR RMS did not change between conditions ($p = 0.564$). FCU RMS did not change between conditions ($p = 0.863$).

**Performance Measures**

Improvement in performance measures after IPC was not observed in this study. The handgrip test in the present study was modeled after a previous study who utilized 13 healthy men. Barbosa and colleagues demonstrated a significant increase in time to task failure (TTF) in the handgrip test after IPC of approximately 20 seconds or 11% (IPC: 198 ± 70 s; SHAM 179 ± 66) (Barbosa et al., 2015). In contrast, the present study did not demonstrate any significant improvement in TTF in the handgrip test after IPC (Table 1, Figure 1). Although the findings from this present study found that there was approximately a 5 minute increase in average performance, this was insignificant due to only one participant who improved performance by around 17 minutes. Participant's individual TTF performance is demonstrated in figure 2. The average TTF in the study done by Barbosa and colleagues was around 3 minutes total (including SHAM and IPC conditions). The overall shortest TTF in this present study was around 9 minutes total (including SHAM and IPC conditions). These opposite findings could be due to different subjects utilized for each study. This present study included both male and female participants who had a SCI. Barbosa et al., 2015 utilized healthy able-bodied males only.

The differing findings could also be due to the difference in muscle structure and adaptations between the healthy able-bodied individuals and the individuals who have experienced a SCI. The shortest TTF of the handgrip test in this present study was 9 minutes, and the previous mentioned study utilizing able bodied subjects reached a maximum TTF of the handgrip test of around 6 minutes. Studies who have compared upper body strength in both of these populations have demonstrated that wheelchair users have increased strength compared to able bodied individuals (Cobanoglu et al., 2020, Külünkoğlu et al., 2018, Mayer et al., 2001). A specific study comparing handgrip strength in able bodied individuals to wheelchair users with similar demographics demonstrated an increase of around 24% in handgrip measures for the individuals who used wheelchairs as primary transportation (Külünkoğlu et al., 2018).

The only study utilizing a similar subject group as the present study had participants perform a maximal arm crank fatiguing test. They compared the effects of IPC on lower limbs and upper limbs before the arm crank task. It was demonstrated that this specific population, with no lower body functioning due to injury site location being a complete thoracic injury, only benefits from intervention that is on the limb performing the task. They saw no improvements when IPC was applied at a remote location (Seeger et al., 2015). Due to the findings of this study, the present study applied IPC to the arm that was engaging in the exercise task. This differs from able-bodied studies utilizing the intervention locally or more remote whose findings demonstrated benefits to performance regardless of location (Cheng et al., 2021; Crisafilli 2011; Cruz et al., 2015; Cruz et al., 2016; Griffin et al., 2019; Halley et al., 2020; Jean St-Michel et al., 2011; Paradis-Deschênes et al., 2020; Patterson et al., 2015; Tomschi et al., 2018). This earlier study utilizing individuals with a SCI demonstrated that IPC 662 ± 176 s increased performance times in comparison to SHAM conditions 636 ± 184 s ($p = 0.05$). This present study, although it had similar participant characteristics, did not have these findings.

The most notable difference may be the exercise task. An arm crank test is an aerobic exercise task that requires output from both arms, increased blood flow and includes more muscular contribution from the entire upper limbs compared to an intermittent isometric handgrip test that requires one arm and a smaller focused muscle group. Due to a majority of studies that demonstrated benefit in performance measures after IPC requiring larger muscle group expenditure to perform the given task, it is up for discussion if IPC is able to improve capability in tasks that require more focalized individual muscular output. Secondly, another difference is that this study only included a specific type of SCI, being complete thoracic. This present study was inclusive of all injury site locations and included individuals who had both cervical and lumbar injury sites.

**Muscular Force**

This study demonstrated that muscular force was not influenced by IPC. In contrary, a study utilizing stroke survivors found an increase in MVC values by an average of 16% after IPC intervention. In common with the present study, participants received the cuff intervention on the same limb performing the task at hand (MVCs). Although both of these conditions affect the central nervous system and result in a form of neurological impairment either temporary or long term, it's possible that the differences in their clinical implications could be due to the opposing results. A stroke occurs within the blood vessels where oxygen supply is reduced or blunted to the brain. This may result in permanent damage, but also may be partial and therefore the vessels would still be responsive to the vasodilatory mechanisms associated with IPC. A SCI occurs within the vertebrae in the spinal column affecting the tissues, nerves, and bones in that region. This causes limited or completely impaired connection with the nerve communication to the brain. This results in either partial or complete disruption within the functioning of neurons. Although mechanistic contributions are not solidified in the literature, it is suggested that IPC improves oxygen delivery and blood flow (Andreas et al., 2011; Barbosa et al., 2015; Cheng et al., 2021; Griffin et al., 2019; Kimura et al., 2007; Paradis-Deschênes et al., 2020; Patterson et al., 2015; Tomschi et al., 2018). If this is the case, since the consequences of a stroke occur within the blood vessels which may be partially damaged, but yet responsive vessels, this could be why a significant benefit was seen within the stroke participants. It is possible that IPC restores the communication between damaged vasculature who experience acute blunting from the stroke occurrence and why these same results are not seen with individuals who have experienced a SCI. Damage after an SCI oftentimes is more permanent. The nerves are completely severed and there is no opportunity for restoration. Therefore, the reparative response from IPC was not demonstrated in this present study with individuals who have experienced a SCI.

Additionally, another differing factor other than the subject population was the cuff location. Due to Hyngstrom et al., 2018 having the participants experience the cuff intervention on the lower limbs, it is possible that this contributed to the beneficial performance measures in comparison to this present study where the cuffs were on the upper limbs and there was no improvement in performance measures. The leg muscles have more mass in comparison to the arm, and it has been speculated that the amount of muscle mass and tissue that is exposed to the IPC has an impact on if benefits are obtained and how much (Barbosa et al., 2015; Lamidi et al., 2021).

**Neural Measures**

This present study did not find any evidence supporting that there is a neural benefit obtained from IPC, and there was no significant change in recorded sEMG values. Although the mechanism influencing performance improvements from IPC is still up for discussion, previous studies with able-bodied population have demonstrated IPC delays fatigue, allows for more efficient output, and decreases the feeling of pain during performance, reported by RPE (Barbosa et al., 2015; Cheng et al., 2021; Crisafulli 2011; Halley et al., 2020; Jean St-Michel et al., 2011; Patterson et al., 2015; Tomschi et al., 2018) suggesting that there is an increase of neural recruitment after intervention.

Supporting results of increased muscle activation demonstrated in sEMG potentials during an exercise task after IPC was displayed in aerobic cycling (Cruz et al., 2015; Cruz et al., 2016). sEMG activity of the vastus lateralis was 9.7% higher after IPC compared to SHAM ($p = 0.017$). Additional findings demonstrated attenuation in ratings of perceived exertion during overall performance ($p = 0.01$). It was speculated that these results were due to an increase in voluntary neural drive from motor neuron activity and decreased sensitivity of the body's fatigue signals. Although this present study split the performance test (i.e. the handgrip test) in 6 different timepoints (BL, 20%, 40%, 60%, 80%, 100%) which is a different breakdown than the study being discussed, similar results were not demonstrated. This present study did not see increased sEMG activity of either muscle being recorded, the FCR (p=0.564) and FCU (p= 0.863) when compared to SHAM. The difference of sEMG activity after IPC compared to SHAM conditions had a lot of variability in individual values. Other than differing participant characteristics, it's possible that the varying tasks could have led to these opposing results. Cycling is a repetitive aerobic task that requires a larger contribution aerobically compared to the isometric submaximal contraction handgrip test in this present study that requires no aerobic contribution. This leads to speculation on if demonstrated neural contributions found are a result of an increased capacity of recruitment for oxygen delivery. Multiple investigators have supported the findings that IPC leads to increased oxygen to the working muscle and a majority of the tasks utilized require a greater aerobic contribution (Andreas et al., 2011; Barbosa et al., 2015; Cheng et al., 2021; Griffin et al., 2019; Kimura et al., 2007; Paradis-Deschênes et al., 2020; Patterson et al., 2015; Tomschi et al., 2018).

Increased sEMG activity was also demonstrated in stroke survivors where RMS magnitude of the vastus lateralis resulted in an increase of 30.7 ± 15% after IPC (p= 0.01) during MVCs. The authors suggest that IPC stimulates muscle afferents group III and IV that are reactive to ischemia. This response engages brainstem centers to release neuromodulators known to increase the excitability of spinal motor neurons. They speculate that since these afferent group pathways in the paretic leg after a stroke are shown to be hyperexcitable, this factor could be an attribution to the positive results demonstrated in this specific group (Hyngstrom et al., 2018).

Additionally, Barbosa et al., 2015 study findings found that IPC attenuated the slowing of contraction and relaxation rates indicated by values at peak exercise resulting in 637 N/s after IPC and 587 N/s after SHAM, a 8.7% difference in the continuous handgrip test and increased the rate of force development. They attributed these results to an adapted more efficient neural processing of excitation-contraction coupling.

Opposing these findings, more recent studies did not find any influence of neural recruitment in recorded sEMG potentials leading to performance increases demonstrated (Halley et al., 2018; Halley et al., 2019) in both aerobic and anaerobic tasks. It was postulated that these differing findings were mostly due to different performance measure tasks and participant characteristics among present studies. In a series of studies, Halley and colleagues utilized highly trained individuals who have adapted to maximal muscle mass recruitment patterns while exercising (Halley et al., 2018; Halley et al 2019). Similar to the participants in this present study, these individuals have adapted their upper body musculature to compensate for the lack of functioning in the lower limbs. They are maximally recruiting these constantly working muscles in the upper limbs. This could be why positive results were not demonstrated and give reasoning to the studies that found positive outcomes. The studies mentioned above used untrained healthy individuals and individuals who have experienced a stroke. These groups of subjects are different from the two mentioned above, due to training level and impairment. They are not maximally recruiting during their exercise task and have room for increased muscle recruitment patterns as a result of the IPC.

Within this present study's subject population, it is up for question if there was further investigation on individuals with some functioning of the lower limbs and if benefit would be demonstrated from IPC. Positive results could be supported due to the legs not maximally recruiting and having limited functioning. Benefits obtained from IPC could be dependent on the recruitment pattern for specific muscle groups.

**Limitations**

As mentioned above, the main limitations for this study was the lack of data collection leading to inconclusive significance of findings. More data is needed to determine the validity of these results. The previous study investigating the effects of IPC on individuals with spinal cord injury only included individuals with an injury site in the thoracic region. Another limitation is that similar studies use a homogeneous subject pool, and with this current study, the participants are a heterogeneous group. This is due to the varying levels of spinal cord injury. Individuals vary upon specific injury location on the spinal column as well as varied functioning levels and individualized impairments. This study had participants with injury site locations in both the cervical and lumbar region. With these differences, IPC could have a different effect on each individual depending on their individual abilities. Additionally, a common limitation among studies using IPC is the lack of ability to truly blind a subject of the different pressures and feelings from the IPC compared to SHAM intervention. To reduce bias, participants were told that this study was trialing out two different cuff pressures that have both been demonstrated to improve performance.

**Conclusion**

In conclusion, the main outcome found was that IPC did not improve performance output. Secondly, there was no evidence to demonstrate improved neural recruitment after IPC condition compared to SHAM. These results can lead to speculation on further investigation on how IPC influences individuals with a neurological injury, specifically those who have experienced a spinal cord injury.

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# APPENDIX A

# MEAN AND STANDARD DEVIATIONS OF MVC VALUES

Table 1

Mean and Standard Deviations of MVC Values

| | SHAM | IPC |
|---|---|---|
| BL | 608.67 ± 251.48 | 676.69 ± 245.89 |
| Post-HGT | 556.52 ± 207.93 | 584.64 ± 197.46 |
| Post-HGT & INT | 534.32 ± 210.89 | 571.38 ± 241.83 |

Table 1 represents the mean and standard deviation of the MVC values at the different time points for both IPC and SHAM (inactive procedure that mimics the actual IPC condition) conditions. IPC 1 and SHAM 1 is the MVC value baseline. IPC 2 and SHAM 2 is the MVC after intervention. IPC 3 and SHAM 3 is after intervention and handgrip test. HGT: handgrip test, BL: baseline, INT: intervention.

# APPENDIX B

# INDIVIDUAL PARTICIPANT CHARACTERISTICS

Table 2

Individual Participant Characteristics

| Participant | Sex | Body mass (kg) | BMI | Location of injury | ASIA Classification | Time since injury (years) | Engagement in 30 mins of physical activity (days) |
|---|---|---|---|---|---|---|---|
| 1 | male | 63.51 | 21.9 | L3 | A | 19 | 4 |
| 2 | male | 70.31 | 21.6 | C5/C6 | D | 11 | 3 |
| 3 | male | 97.52 | 24.2 | T12 | A | 34 | 6 |
| 4 | female | 46.36 | 19.5 | T11/T12 | A | 2 | 1 |

Table 2 represents the individual characteristics of the participants.

# APPENDIX C

# TIME TO FAILURE (TTF)

Figure 1

Time to Failure (TTF)

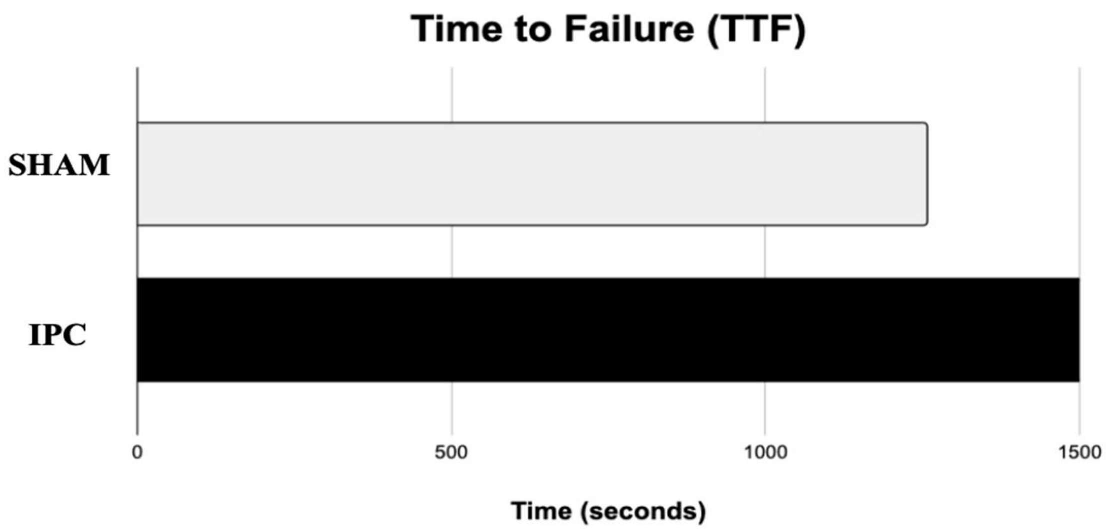


Figure 1 represents the average value (M ± SD) of time to task failure (TTF) for the handgrip test. SHAM: sham intervention IPC: ischemic preconditioning.

# APPENDIX D

# INDIVIDUAL TTF VALUES

Figure 2

Individuals Time to Failure (TTF) Values

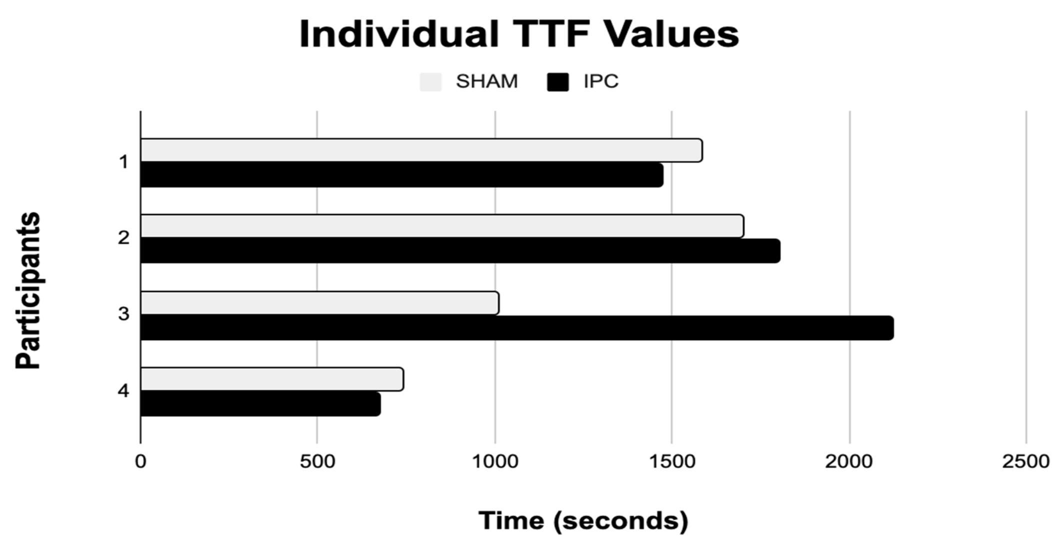


Figure 2 represents the individual values of time to failure (TTF) for the handgrip test. SHAM: sham intervention IPC: ischemic preconditioning intervention.

APPENDIX E

MVC VALUES

Figure 3

MVC Values

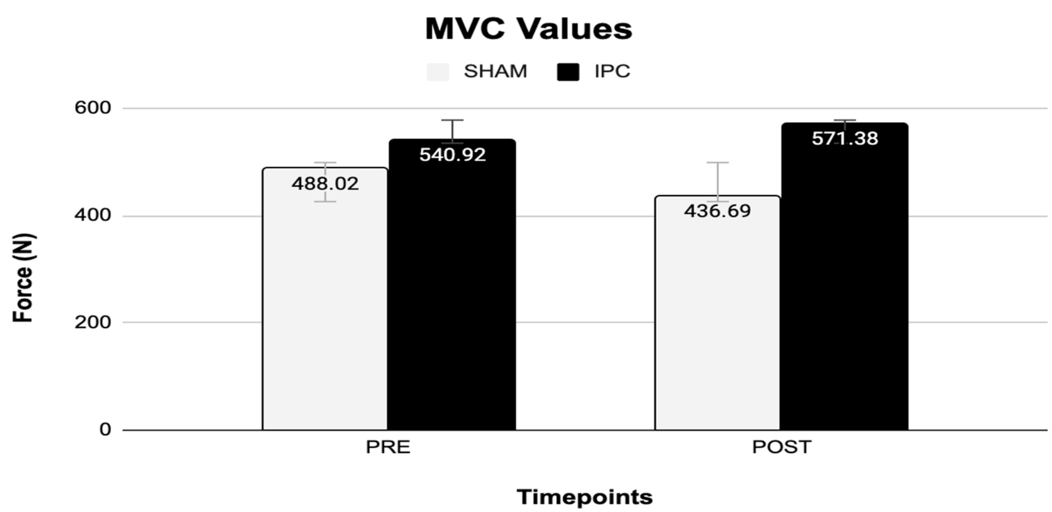


Figure 3 represents the average value (M ± SD) of maximal voluntary contraction (MVC) measures at the two different timepoints. PRE: baseline measures, POST: at the end of the experimental session after intervention, IPC: ischemic preconditioning

# APPENDIX F

## AVERAGE PERCENT CHANGE IN RMS OF THE FLEXOR CARPI RADIALIS

Figure 4

Average Percent Change in RMS of the Flexor Carpi Radialis

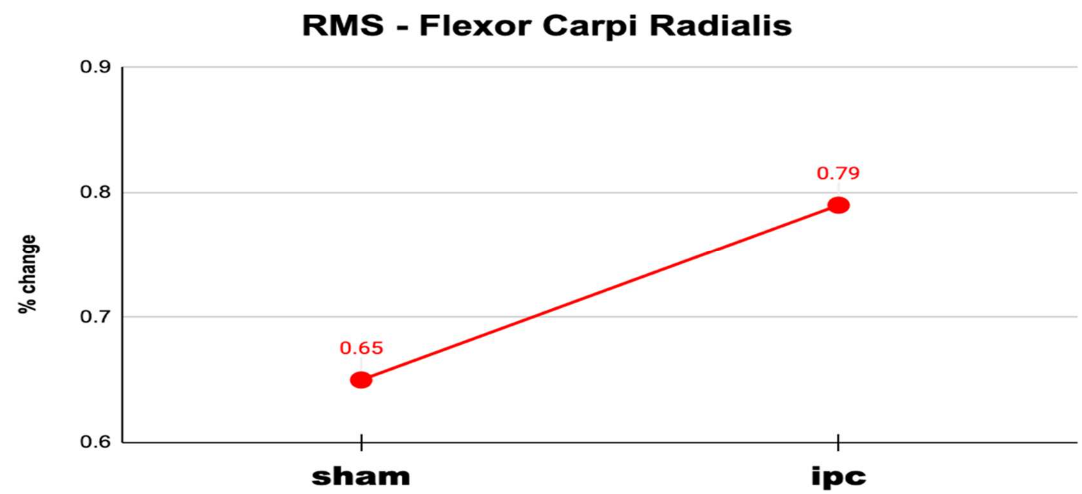


Figure 4 represents the average percent change values for the RMS recording of the flexor carpi radialis muscle which was recorded during the TTF handgrip test. Percent change was calculated based off of the difference in the baseline recordings and 100% recordings. RMS: root mean square, IPC: ischemic preconditing