ULISSES TIROLLO TADDEI

Efeitos de exercícios terapêuticos para o complexo tornozelo e pé na incidência de lesões, na funcionalidade e saúde dos pés em corredores fundistas: um ensaio clínico randomizado

Tese apresentada à Faculdade de Medicina da Universidade de São Paulo para obtenção do título de Doutor em Ciências

Programa de Fisiopatologia Experimental

Orientadora: Profa. Dra. Isabel de Camargo Neves Sacco

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Dedico este trabalho aos meus pais

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NORMATIZAÇÃO ADOTADA

Esta tese está de acordo com as seguintes normas, em vigor no momento desta publicação:

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Introdução: Sua fácil acessibilidade fez com que a corrida de longa distância fosse praticada em todo o mundo. Sua popularidade continua crescendo por seus benefícios à saúde e qualidade de vida. Nos últimos anos, o fortalecimento dos músculos pé e tornozelo tem sido o foco de alguns estudos para a prevenção de lesões relacionadas à corrida, denominando esta abordagem terapêutica – Bottom-up, em oposição a tradicional Top-down que aposta no fortalecimento dos músculos do Core. Esta tese compõe um conjunto de estudos, cujo centro é um estudo randomizado, prospectivo, controlado e paralelo (ClinicalTrials.gov NCT02306148) com avaliador cego e follow-up de um ano, que visaram responder alguns objetivos: (1) avaliar a viabilidade do ensaio e do protocolo de exercício proposto, (2) avaliar a eficácia do protocolo em alterar a saúde e funcionalidade dos pés-tornozelos, o trofismo dos músculos plantares, e a biomecânica da corrida, e (3) verificar os efeitos do protocolo na incidência de lesões relacionadas à corrida em corredores recreacionais. **Métodos**: Esta tese foi composta pela compilação de dois artigos publicados (Physical Therapy in Sport) e um submetido (British Journal of Sports Medicine). O primeiro artigo abordou a viabilidade do ensaio clínico e do protocolo de exercícios. E o segundo artigo foi uma prova de conceito com 28 corredores investigando a eficácia da intervenção no fortalecimento dos músculos dos pés, na funcionalidade de pé e tornozelo e na alteração da biomecânica da corrida. O manuscrito submetido com os resultados finais investigou as diferenças de incidência de lesões e análise de sobrevida após um ano de acompanhamento com os 118 participantes. **Resultados:** O estudo de viabilidade mostrou que o laboratório possuía a capacidade de avaliar 20 corredores semanalmente e que os dados coletados estavam adequados para processamento e analise. 702 corredores se mostraram interessados em participar do estudo e após uma triagem inicial 155 não passaram nos critérios de elegibilidade. No estudo de prova de conceito constatou-se que o protocolo de exercício aumentou em média 15,2% os músculos intrínsecos estudados e o impulso propulsivo durante a corrida em 3% no grupo intervenção sem alterações notadas no grupo controle. Os resultados da análise de sobrevida ao fim de 12 meses de follow-up mostraram um risco 2.42 vezes maior de ocorrência de lesões no grupo controle comparado ao grupo intervenção. **Conclusão**: O ensaio clínico proposto foi considerado viável com corredores dispostos a participar da pesquisa e com boa aderência ao protocolo. O protocolo de exercício baseado na abordagem *Bottom-up* foi eficaz, aumentando o volume dos músculos intrínsecos investigados e modificando a biomecânica de corrida, aumentando o impulso vertical durante a propulsão. O fortalecimento dos músculos intrínsecos do pé diminuiu a incidência de lesões relacionadas a corrida em corredores recreacionais.

Descritores: Corrida; Fenômenos biomecânicos ; Traumatismos em atletas; Pé; Treinamento de resistência; Incidência.

ABSTRACT

TADDEI UT. *Effects of therapeutic exercises for the foot/ankle complex in the incidence of injuries, functionality and foot health in long distance runners:* a randomized clinical trial [thesis]. São Paulo: "Faculdade de Medicina, Universidade de São Paulo"; 2019.

Introduction: The easy accessibility made long-distance running to be practiced worldwide and its popularity continues to expand with the growing interest for health and quality of life improvement. Over recent years, strengthening the foot-ankle muscles have been the focus of some studies for the prevention of running-related injuries, naming this therapeutic approach as – Bottom-up, opposed to the traditional Top-down approach that wages on strengthening the proximal Core muscles. This thesis is composed by a set of studies whose core is a randomized, prospective controlled and parallel trial (ClinicalTrials.gov NCT02306148) with blind assessment and follow-up of one year, following a bottom-up approach, with the main objective to test its effect on running related injury incidence in recreational runners, running biomechanics and foot-ankle functionality. The aim was to assess the following: (1) evaluate the feasibility of the proposed ground-up exercise protocol and the clinical trial, (2) to evaluate the effectiveness of the protocol on foot-ankle health and functionality, foot muscle trophism, and running biomechanics, and (3) verify the effects of the protocol on the incidence of running related injuries in recreational runners. **Methods**: This thesis is presented as a compilation of two published scientific papers (Physical Therapy in Sport) and one submitted (British Journal of Sports Medicine). The first paper approached the feasibility of the clinical trial. The second paper was a proof of concept with a sub sample of 28 runners which investigated the effectiveness of the intervention on strengthening foot muscles and altering running mechanics. The submitted manuscript with the final results investigated the incidence differences and survival analysis after a one-year follow up with 118 participants. **Results**: The feasibility study showed that our laboratory assessment capacity of evaluating 20 corridors weekly was found adequate to the calculated sample size of 112 subjects and that the collected data was adequate for processing and analysis. 702 runners were interested in participating in the study and after an initial screening 155 did not pass the eligibility criteria and 118 were assessed. In the proof-of-concept study, it was found that the exercise protocol significantly increased the intrinsic muscles studied by 15.2% and the propulsive impulse during running by 3% in the intervention group with no changes noted in the control group. The results of the survival analysis at the end of the study showed a 2.42 times greater risk of occurrence of injuries in the control group compared to the intervention group. **Conclusions**: The proposed clinical trial was feasible with runners willing to participate in the research and good adherence to the protocol. The exercising protocol based on the Bottom-up approach was effective in enhancing plantar muscles volumes and changing running mechanics, increasing vertical impulse during push-off. Strengthening the intrinsic foot muscles decreased the incidence of RRIs with a 2.42-fold in recreational long-distance runners.

Descriptors: Running; Biomechanical phenomena; Athletic injuries; Foot; Resistance training; Incidence.

1. INTRODUCTION

1.1. Recreational running as a physical activity

Running is a task inherent to our motor development as we evolved beyond the need of hunting a prey or escaping a predator (Bramble and Lieberman, 2004). It is the physical activity of choice for most individuals mainly due its low cost, convenience, and versatility (Taunton *et al.*, 2002a, 2003; Paluska, 2005). Besides the incontestable health benefits of regular practice of physical activities (Chakravarty *et al.*, 2008; Garatachea *et al.*, 2015; Hespanhol Junior *et al.*, 2015; Vivar and van Praag, 2017), the joy in practicing them increasingly drew people to recreational sports, and recreational running has been one of the most worldwide practiced physical activities with exponential growing interest over the past decades (Chakravarty *et al.*, 2008; Hespanhol Junior *et al.*, 2015).

Although it was reported that in the past three years, participation in street races has declined 13% in Europe and North America, it still counts with a huge number of runners worldwide. In the world, the latest estimate by RunRepeat.com (Jakob Andersen, 2020) is that around 7.9 million runners are engaged in street races in 2019, an increase of 57.8% in the past 10 years. It is estimate though that in the United States alone more than 40 million people run regularly (Videbæk *et al.*, 2015).

In São Paulo state, participation in running events had shown an increase in the past decade going from 372.thousand to 724 thousand participants. The participants trends for race distances are 5 and 21 kilometers

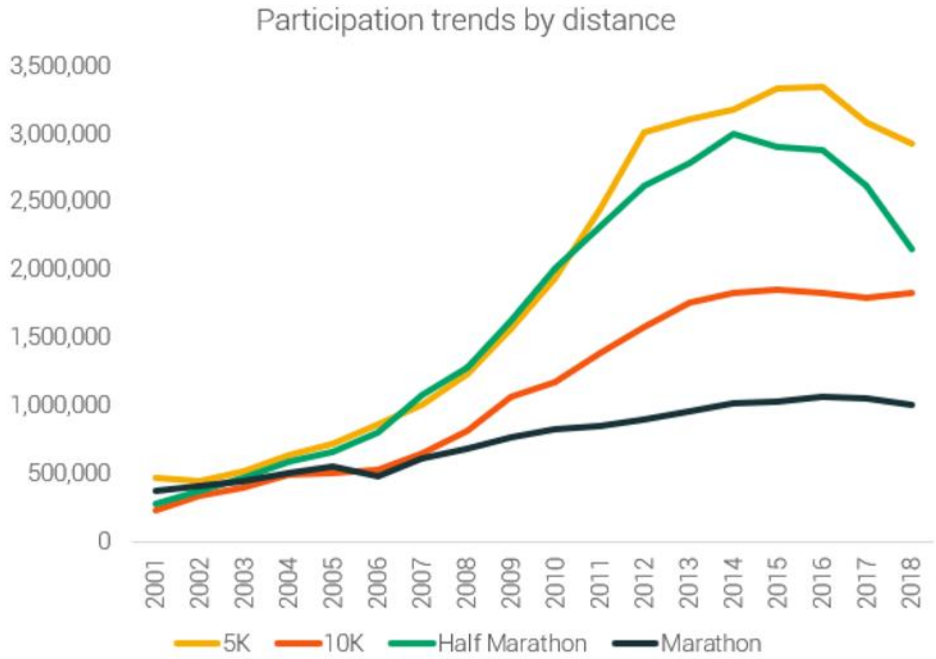

Figure 1. Number of participants in races around the world showing an exponential increase from 2001 to 2011 and a slight decrease in the last two years. Graph taken from https://runrepeat.com/state-of-running.

1.2. Running Related Injuries (RRI)

Unfortunately, there are several running related injuries (RRI) which are usually chronically and impairing Injuries to runners (James, Bates and Osternig, 1978; Taunton, 2003; Van Gent *et al.*, 2007), which lead to discontinuation or interruption of the practice. Even more important is the large incidence of these injuries, varying from 19 to 92% in one year(Van Gent *et al.*, 2007; Saragiotto *et al.*, 2014). This broad incidence interval is a problem of its own. Many authors explaining that this variation is mostly due to the many different RRI definitions used (Van Gent *et al.*, 2007; Yamato, Saragiotto and Lopes, 2015), others mention that the different population studied also influence the incidence reported (Taunton *et al.*, 2002b; Van Der Worp *et al.*, 2015; Videbæk *et* *al.*, 2015; Matias *et al.*, 2016).

The definition of RRI varies considerably across studies, not only regarding the symptoms required to be present to be considered a RRI, but also the amount of time passed since the beginning of the symptoms. Some studies propose that just one day of impaired running practice is enough to qualify a RRI (Buist *et al.*, 2010; Theisen *et al.*, 2014; Malisoux *et al.*, 2015), while others require one week (Lysholm and Wiklander, 1987; Bennell *et al.*, 1996; Buist *et al.*, 2008; Bredeweg *et al.*, 2012).

Another aspect of bias when comparing incidence and prevalence of RRI among studies is the particularities of the population studied. As an example, in studies trying to verify differences between barefoot and shod walking and running, while habitual barefoot populations are hard to find, some studies tend to either investigate indians (Rao and Joseph, 1992; D'Aout *et al.*, 2009), africans or mexican tribes (Lieberman *et al.*, 2010; Holowka, Wallace and Lieberman, 2018). Another example is including in the sample study, military recruits. The internal validity of studies involving military recruits in undoubtedly high due sample homogeneity, high number of participants, almost guaranteed adherence, compliance, and low drop out (Popovich *et al.*, 2000; Knapik, Brosch, *et al.*, 2010; Knapik, Trone, *et al.*, 2010). However, by the same reasons, external validity tends to be very low.

In order to choose a RRI definition for this thesis, we previously established some criteria to search in the literature the best definition. The criteria were as follows: (i) a definition that achieve a middle ground among the majority of the high quality studies; and (ii) a definition that become possible a comparison between our results and most of the results in the literature, especially regarding the time of follow up (events in one year). Matching these criteria established, the definition from of Macera et al. (Macera *et al.*, 1989) was adopted. It stated that a RRI is any musculoskeletal pain or injury that was caused by running practice and that induces changes in the form, duration intensity or frequency of training for at least 1 week.

When reporting the incidence of RRIs, two high quality studies stand out. The first is the literature review by van Mechelen (van Mechelen, 1992) That reports an one-year incidence rate varying between 37 and 56%. Between 50 to 75% of all RRIs happen due to the constant repetition of the same movement and the recurrence rate varies between 20 to 70%. The author concluded that RRI lead to a reduction in the running training or a running cessation in about of 30 to 90% of all RRIs.

The second study about RRI incidence is the systematic review by Van Gent et al (Van Gent *et al.*, 2007). The authors reported an overall incidence of lower extremity injuries varying from 19.4% to 79.3%. The most common site for RRIs was the knee, ranging from 7.2 to 50.0% of the injuries, followed by the lower leg (9.0% to 32.2%), the foot (5.7% to 39.3%), the upper leg (3.4% to 38.1%), the ankle (3.9% to 16.6%) and last the hip/pelvis (3.3% to 11.5%). The large range of the intervals was explained by the authors as a result of the heterogeneity of the studies pooled.

1.3. Risk Factors for RRIs

The investigation of conditions and behaviors that result in RRIs has provided several different conclusions on what possible risk factors might be important for recreational runners, however the studies present different risk factors and they do not agree between them (Wen, 2007; Van Middelkoop *et al.*, 2008; Buist *et al.*, 2010;

Saragiotto *et al.*, 2014; B. Kluitenberg *et al.*, 2015; Van Der Worp *et al.*, 2015; Hulme *et al.*, 2017; Zaar *et al.*, 2017; Becker, Nakajima and Wu, 2018).

Saragiotto, Yamato and Lopes (Saragiotto, Yamato and Lopes, 2014) performed an observational study interviewing 95 runners between 19 and 71 years asking “What do you think can cause injuries in runners?”. The authors divided the possible risk factors in intrinsic and extrinsic, finding that the most frequently reported factors leading to an RRI were related to training, running shoes, and respecting the body’s limitations.

However, a systematic review by Hulme et al. (Hulme *et al.*, 2017), investigating possible risk factors for RRIs, reported that out of the most mentioned factors in the literature (frequency, pace and interval, body weight and body mass index, dietary plan and hormonal status, use of orthotics, stretching, warming up, cooling down, surface, etc.) only a previous RRI and irregular or absent menstruation were associated with an increased risk of RRI. The reason for so many other risk factors, which sometimes were found to be relevant, had been left out was that the quality of most studies reviewed was wanting, and definitive conclusions could not be made.

Understanding the risk factors associated with RRI can provide important benefits for runners. Noteworthy factors include running biomechanics and muscle functionality of the lower extremities, particularly in the feet. A systematic review by van der Worp et al.(Van Der Worp *et al.*, 2015) included 11 high-quality longitudinal studies and concluded that alterations in the biomechanical force distribution patterns, amount of training, history of previous RRI, increased index of the navicular drop, and the misalignment of the ankle, knee, and hip are among the main intrinsic risk factors for RRIs. In addition, extrinsic factors such as the training surface and the type of footwear are also relevant risk factors.

Out of these seven diverse risk factors, two are related specifically to the foot-ankle complex, demonstrating the importance of maintaining the health and functionality of its musculoskeletal structures to prevent injuries. It is also believed that any biomechanical alteration in the musculoskeletal system, in particular the foot-ankle complex, broadly influences a runner's functionality, predisposing him/her to a lesser or greater extent to injuries, in addition to the possibility of compromising his/her quality of life (Bas Kluitenberg *et al.*, 2015; Mei *et al.*, 2019).

1.4. Interventions and effects on RRIs

Studies investigating the effects of different interventions on RRI incidence are still ongoing based on different assumptions. Buist et al.(Buist et al., 2008) investigated the effects of a graded training program with slow increase in volume, assuming that a rapid increase in running mileage was an important risk factor for RRI. The authors found no differences between the intervention and control groups after the study's completion. Fokkema et al.(Fokkema et al., 2017) designed an online advisor directed to each participant according to their RRI risk factors that included personal factors (Age, BMI, injury history), training factors (volume, surface, stretching), biomechanical factors (cadence and foot landing) and equipment factors (footwear, orthotics). Despite the specificity of the intervention, the authors did not find significant effects of the intervention on the RRI incidence.

A controlled trial investigated if wearing motion control running shoes could minimize the injury risk of recreational runners(Malisoux et al., 2016), under the assumption that foot-ankle posture is a risk factor for RRI (Dowling et al., 2014). Interestingly, they found that overall injury risk was lower in the participants that received those shoes compared to the control group on standard shoes. The authors concluded that with cushioned shoes, better motion control may be needed to limit injury risk and motion control shoes may be helpful. However, one might think: isn't foot-ankle motion control a role of the runner itself? And even if wearing cushioned shoes restrains the runner's capability of movement control or demands more of the foot-ankle muscles, is it possible to directly enhance the runner's movement control through training? Training and strengthening the foot-ankle muscles aiming to improve postural control and balance have already proven to be effective in other populations.

In a study with older people with risk of falling, Mickle et al. linked foot deformities and intrinsic foot muscles weakness to the occurrence of falls and showed that this population can benefit from foot core training (Mickle et al., 2016). Goldman (Goldmann and Brüggemann, 2012) showed that the young athletes presented a significant improvement on jump performance after isometric training of the hallux flexion for seven weeks. Sulowska et al(Sulowska et al., 2019) showed in a controlled clinical trial with 47 long-distance runners that a 6-week exercise protocol focusing on the foot-ankle muscles was capable of improving the energy being transferred through the body and power during running measured in a Running-Based Anaerobic Sprint Test (RAST)(Mølgaard et al., 2018).

These studies demonstrate the benefits of strengthening the foot core muscles and, knowing the intrinsic foot muscles role in dampening impacts and propel the body during running (Ker *et al.*, 1987; Kelly, Cresswell and Farris, 2018; Riddick, Farris and Kelly, 2019), it is logical to think that these roles are also going to be improved if trained. Thus, by reducing shock, cumulative load, better controlling foot-ankle motion and alignment, strengthening the foot muscles may result in preventing RRI. Therefore, the aim of this randomized single-blind controlled trial was to verify the effects of a foot muscle strengthening protocol on the incidence of RRI in recreational runners in a one-year follow-up.

2. OBJECTIVES

2.1 Main Objective

The general goal of this thesis was to contribute to the understanding and comprehension of causes for RRI and investigate the role of foot core muscles on the running injury mechanism. Thus, the main objective of this study was to verify if the strengthening protocol developed for intrinsic foot core muscles (ANNEX 1) was capable of reducing the incidence of RRI in the population of healthy recreational long-distance runners.

2.2 Specific Objectives

The specific aims are related to the three manuscripts submitted and published that are being included in this thesis, in the following order:

i. Investigate if the proposed exercise protocol and the randomized control trial planned were viable and feasible in terms of accessibility to participants and recruitment success; participants' satisfaction and adherence to the program; and effective on changing foot muscle strength and foot biomechanics;
ii. Verify whether the foot exercising protocol is capable of strengthening the intrinsic foot muscles of recreational runners, and if it is capable of altering the participants' running biomechanics;

iii. Investigate the effects of the foot exercising protocol on RRI incidence in recreational long-distance runners and identify the risk of developing a RRI between the intervention and control groups.

2.3 Hypothesis

Our hypotheses related to all three specific objectives are that the therapeutic exercise protocol for the foot-ankle (ANNEX 1) as practiced by long-distance recreational runners:

H 1. Is feasible, accessible to the population, positive in its effect and the population adheres positively to the program (specific objective i),

H 2. Increases intrinsic foot muscle strength (specific objective ii),

H 3. Increases foot muscle cross-sectional area and volume (specific objective ii),

H 4. Improves foot health and functionality status (specific objective ii),

H 5. Reduces dynamic strain on the foot's longitudinal arch during running (specific objective ii),

H 6. Reduces the incidence of RRIs in the lower limbs in one-year follow-up (specific objective iii),

H 7. Lengths the time for the occurrence of the first RRI in the lower limbs in one-year follow-up (specific objective iii).

3. METHODOLOGY

The results of this thesis have already been published in two papers and submitted in another manuscript that is under review. Therefore, this thesis is presented as a compilation of two published scientific papers and one submitted, reproduced in the following sections.

The first study has been published in Physical Therapy in Sport in 2018 (impact factor = 2.00) and presents the results of the feasibility study of the RCT protocol proposed in 2016 (Matias et al. 2016). In this paper, we investigated the accessibility of the participants to the study; the success in recruiting subjects for the clinical trial; the satisfaction and adherence of the participants to the intervention and the effect of the intervention in changing the foot strength, functionality and running biomechanics. This feasibility study was also used as a preliminary study to estimate the sample size for the clinical trial (Taddei *et al.*, 2018).

The second study was also published in in Physical Therapy in Sport (impact factor = 2.00) in 2019 and is a proof-of-concept to test whether the foot exercise protocol proposed for recreational runners is really effective in strengthening the foot intrinsic musculature and results in changes in running biomechanics, as well as in functional aspects of the longitudinal plantar arch (Sacco, Taddei and Matias, 2019).

The third paper submitted to the *British Journal of Sports Medicine* (impact factor =11,0) in 2020 shows the main outcomes of the clinical trial - RRI incidence after the intervention proposed. In this paper, we present a survival analysis of recreational runners who underwent the foot exercise protocol regarding RRI, and we compared the risk of injury in this intervention group with a control group, both followed for a period 12 months (Taddei et al. 2020, under review).

Additionally, a year research internship was included as part of the PhD project development, which took place at the Spaulding National Running center in (Cambridge, USA) at the Harvard Medical School, supervised by professor Dr. Irene Davis. During the internship, I was trained by the laboratory staff to collect, process and analyze data from instrumented treadmill, force platforms, motion capture infrared cameras and inertial measurement units. The training involved MATLAB software programing and Visual 3D processing following the Spaulding biomechanics laboratory *modus operandi* on assessing runners for their normative database. This database was constantly been statistically explored over the supervision of Dr. Davis. We also design a cohort study with a one-year monthly follow up with the title "Effects of foot strength and footwear in one-year running injury incidence: a prospective study". The purpose of this study was to compare running mechanics, foot strength and injury pattern of long-distance runners habituated to minimal shoes, partial minimal shoes and standard running shoes. I recruited and assessed 20 runners until the end of my stay and the project is still ongoing.

4. PUBLISHED PAPER 1

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Original Research

Effects of a therapeutic foot exercise program on injury incidence, foot functionality and biomechanics in long-distance runners: Feasibility study for a randomized controlled trial

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Background: The goal was to examine the feasibility of a randomized controlled trial (RCT) on the effect of a therapeutic foot-ankle training program to prevent injury in long-distance runners. First, we eval- uated (i) the access to participants and recruitment success; (ii) participants' satisfaction and adherence to the program; (iii) the effect of the training program to improve foot muscle strength and change foot biomechanics; and, second, we used the collected data for a post hoc sample size calculation.

Methods/design: We randomized 31 healthy long-distance recreational runners to either an 8-week foot-ankle muscle strength-training program (intervention) or a stretching protocol (control). The recruit- ment rate was the number of eligible participants per week of recruitment; recruitment success, the ratio between scheduled baseline visits and initially eligible participants. Participant satisfaction was assessed by a questionnaire, and adherence to the training program was recorded in a Web-based software, both at the 8-week mark. Program effect was assessed by hallux and toe muscle strength using a pressure platform, foot muscle cross-sectional area using magnetic resonance imaging and foot kinematics during running using 3D gait analysis; assessments were done at baseline and after 8 and 16 weeks. A post hoc power analysis was performed on foot strength and the biomechanical data was collected.

Results: In two weeks of recruitment, 112 initially eligible subjects were screened, 81 of whom were deemed eligible and 31 had a baseline study visit, giving a recruitment rate of 40.5 subjects/week and recruitment success of 28%. Participants' adherence was 97%, and satisfaction scored a median >3 out of 5 on a Likert scale on all questions. The cross-sectional area of the abductor hallucis (P ¼ 0.040) and flexor digitorum brevis (P ¼ 0.045) increased significantly at 8 weeks in the intervention group. The post hoc sample sizes for almost all the strength and biomechanical parameters were below those of the 112 subjects calculated as the original sample size for clinical outcome (running-related injury).

Conclusion: Results show that this RCT is feasible, given an accessible study population that is willing to participate and that perceives the training program as positive and adheres to the program. The training program leads to several positive outcomes on muscle strength that justifies assessing clinical outcomes in this RCT.

1. Introduction

The foot ankle complex has long been known for its capacity to absorb shock, adapt to terrain, support bodyweight and propel the body during walking and running in healthy conditions (L. A. Kelly, Kuitunen, Racinais, & Cresswell, 2012; Mckeon, 2015; Mckeon, Hertel, Bramble, & Davis, 2014). These capacities are connected to the intrinsic foot muscles, whose main functions are to maintain

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1. Introduction

The foot-ankle complex has long been known for its capacity to absorb shock, adapt to terrain, support bodyweight and propel the body during walking and running in healthy conditions (Kelly et al., 2012; Mckeon et al., 2014; Mckeon, 2015). These capacities are connected to the intrinsic foot muscles, whose main functions are to maintain the foot arches, absorb, dissipate and return kinetic energy, and generate power and torque the foot arches; absorb, dissipate and return kinetic energy; and generate power and torque during locomotor activities (Fukano & Fukubayashi, 2009, pp. 387e392; Spink et al., 2011). In running, high demands are placed on these muscles, because the required forces to perform such activities are increased in both intensity and duration compared with a regular locomotor task. Evidence shows that when these intrinsic foot muscles are weak or dysfunctional, the mentioned capacities might be compromised (Nigg, 2009), increasing the load on other passive structures, such as the plantar fascia, promoting excessive pronation, compromising the performance of various activities and increasing the incidence of foot deformities (Kaufman, Brodine, Shaffer, Johnson, & Cullison, 1999; Mickle, Munro, Lord, Menz, & Steele, 2009; Miller, Whitcome, Lieberman, Norton, & Dyer, 2014) and injuries. An increase in intrinsic foot muscle strength and function to maintain foot structure may enhance the capacity of these structures during highly repetitive loading-cycles, as in running, and possibly delay or even prevent the occurrence of running-related injuries (L. a Kelly, Cresswell, Racinais, Whiteley, & Lichtwark, 2014; Mckeon, 2015). Given that increased pronation is one of the most frequently reported risk factors for running-related injuries (Buist, Bredeweg, Lemmink, van Mechelen, & Diercks, 2010; Dowling et al., 2014; Hetsroni et al., 2006; T. M.; Willems et al., 2006; Tine Mar- ieke; Willems, Witvrouw, De Cock, & De Clercq, 2007), exercise training for the intrinsic foot muscles may help in preventing such injuries. To test this premise, a randomized controlled trial (RCT) to study the effects of foot strength exercises was set up by our research group (Matias, Taddei, Duarte, & Sacco, 2016).

Some researchers have already showed that through exercises, it is possible to enhance foot strength and functionality, even in elderly people, change foot alterations/deformities and improve foot biomechanics (Bennett, Reinking, & Rauh, 2012; Campitelli, Spencer, Bernhard, Heard, & Kidon, 2016; Goldmann, Sanno, Willwacher, Heinrich, & Brüggemann, 2012; Headlee, Leonard, Hart, Ingersoll, & Hertel, 2008; Jam, 2006; Jung, Koh, & Kwon, 2011). Studying the risk factors for running-related injuries and monitoring them for changes by performing exercise training are the first steps in further understanding the causality between these risk factors and injury mechanisms.

However, studying the effects of strengthening the human body involves more than meticulously developing a training protocol. In sports practice, commitment and adherence to a program are essential to benefit from that practice in terms of performance and improved health conditions. In running, the training periodization (volume and strategy) is just as important as the adherence and compliance to the planned scheme. The same applies to a training protocol aimed at improving intrinsic foot muscle strength, which is dependent not only on a well-considered scheme of exercises and frequency, but also on the adherence to the training protocol. Non-adherence may not only limit improvement but also withhold any possible benefits, such as injury prevention. In the clinical trial conducted by Bus et al. (2013) that investigated the effects of orthotics on diabetic foot ulcer recurrence, the benefits of the intervention were not statistically significant until the intervention group was divided according to their adherence to the intervention. This shows how effectiveness can be undermined by an essential condition, such as the motivation of the participants. Measuring adherence beforehand can be a powerful tool in planning and thus conducting a clinical trial.

Of equal importance in investigating the effect of an intervention is the effect size on each variable assessed. A number of studies underestimate the number of subjects needed to draw relevant conclusions about an effect on a variable when a simple calculation of the effect size or a statistical power analysis would suffice on minimizing inferential errors (Conrado de Freitas et al., 2017; Koral, Oranchuk, Herrera, & Millet, 2009; Mizuno, Arai, Todoko, Yamada, & Goto, 2017). In the study of a diverse population such as recreational runners, and not accounting for its huge variability (e.g. response to training), the internal validity of any clinical trial would be compromised. Narrowing down the population by restricting the eligibility criteria compromises external validity, and the conclusions would be restricted to a specific runners' group possibly not representative of the general population of long-distance runners.

The goal of the feasibility study would be to reveal operational and scheduling threats, among other drawbacks, and advantages of the protocol. Our general goal is to conduct a randomized controlled clinical trial on the effectiveness of a therapeutic foot-ankle exercise program on the prevention of lower-extremity in- juries in long-distance runners (Matias et al., 2016). Our goal is to assess the feasibility of this trial, focusing specifically on, first, assessing (i) accessibility to participants and recruitment success; (ii) participants' satisfaction and adherence to the program; (iii) the effect of the training program on changing foot muscle strength and foot biomechanics, as mechanisms that could contribute to injury prevention and, second, using the collected data for a post hoc sample size calculation. In this paper, we described the feasibility of a RCT based on pre-established criteria defined by the CONSORT (Consolidated Standards of Reporting Trials) (Schulz, Altman, Moher, & CONSORT Group, 2010). We emphasize that the results reported in this study have limited external validity and statistical power to infer conclusions beyond the feasibility of the future randomized controlled trial.

2. Methods

2.1. Participants

Recreational long-distance runners were recruited through on- line advertisements (Laboratory of Biomechanics website www. usp.br/labimph) and by directly approaching running clubs located around the university campus. Participants were eligible if they ran at least 20 km per week, were between 18 and 55 years of age, and had no lower limb injury or pain in the two months prior to baseline assessment. Participants were excluded if they were under any physical therapy treatment at baseline, had a history of using minimalist shoes or barefoot running, presented any orthopaedic impairment, had previous lower-limb surgery, presented any neurologic impairment, presented any major vascular complications or had diabetes mellitus.

Participants' eligibility criteria were assessed by an online questionnaire after participants signed up for the research.

This clinical trial was approved by the Local Ethics Committee (Protocol number no. 031/15) and registered in ClinicalTrials.gov Identifier NCT02306148. All runners received an explanation and had been asked to read and sign an informed consent form containing all the details of the study.

2.2. Randomization, allocation and blinding

Blocked randomization was performed based on numbers generated by the random allocation program ClinStat (Bland, 2015). The code for each group was kept in opaque and sealed envelope containing. An independent researcher not involved in the study assigned the participants into the intervention and control groups.

2.3. Intervention protocol

Each subject went through a biomechanical and clinical evaluation at baseline (T0). Availability of acquisition equipment and personnel limited the number of runners that could be evaluated per week to 20. For the intervention group, baseline screening was followed by an 8-week training program for strengthening the muscles of the foot-ankle complex, as was published before in Matias et al. (2016). These runners were trained in weekly sessions by a physiotherapist and instructed to perform the same exercises at home at least twice a week. Runners recorded their training sessions in a Web-based software (www.usp.br/labimph/saec) and additionally completed data on running volume and, in the event of an injury, on the injury symptoms. The researcher had access to the Web-based software and could use this to score protocol adherence and to contact the subject in the event of injury symptoms (“SAEC- Software de Apoio aos Exercícios na Corrida,” n.d.) (Fig. 1).

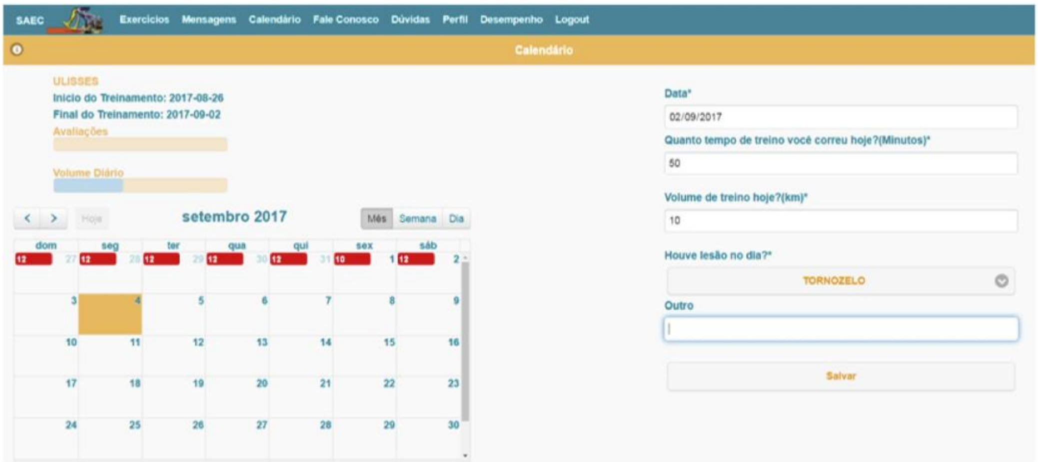

Figure 1. Web-software interface developed to support the exercises training protocol.

The Web-based software contains videos with walkthroughs and descriptions of each exercise of the protocol (Fig. 2), which could be accessed only by a subject with an intervention group login. More details on the strengthening and stretching protocol are available in the published protocol of the RCT (Matias et al., 2016).

Figure 2. Video and description example of an exercise using the web-software. Feature only available for subjects of the intervention group.

In every locally supervised session, the physiotherapist verified if the performance of each exercise was executed according to the protocol, providing help and tips when necessary. After the 8-week training period, each subject was evaluated again (T8) for biomechanical and strength parameters, and the subjects continued the training sessions on their own with the instruction to perform these exercises three times a week until the end of their participation in the RCT, with a one-year follow-up from T0. A final follow- up assessment for biomechanical and strength parameters occurred at 16 weeks (T16).

Subjects in the control group performed a 5-min placebo warm- up and muscle stretching protocol for the duration of the study. This stretching protocol was demonstrated to each subject (Matias et al., 2016) and a list with the description and pictures of each exercise was sent to them by email and mobile phone. Runners in the control group were instructed to access the Web-based soft- ware, entering only data regarding weekly training volume and running-related injury. When a runner failed to access the Web- based software for a full week, the physiotherapist responsible for the training contacted the runner to follow up on this and encourage the runner to complete the data.

2.4. Outcome measurements

For this feasibility study, the main outcomes were recruitment rate and success; participants' satisfaction with and adherence to the training protocol; and the effect of the intervention in improving foot muscle strength and foot biomechanics. We used the collected data for post hoc sample-size calculation on the foot strength and biomechanics parameters. To qualify the study as feasible, adherence to the baseline assessments and to the training protocol between T0 and T8 had to be above 80%, the recruitment rate had to be equal to or greater than the laboratory limitations (20 runners/week) and significant differences in foot strength indicating the effect of the intervention were expected. The dropout rate was calculated as the number of participants who terminated the training program and dropped out of the study.

2.5. Recruitment

Recruitment was assessed by means of calculated rates: recruitment rate and recruitment success. The recruitment rate was calculated as the ratio between the number of eligible runners and the duration of the recruitment period, expressed as runners per week. Recruitment success was calculated as the ratio between the number of scheduled runners for baseline assessment and the number of initially eligible runners to be included in the study, expressed as a percentage. The challenges of the recruitment process will be described qualitatively.

2.6. Adherence and dropping out

Adherence to the training program was calculated as the percentage of training sessions completed by the subject in the intervention group with respect to the total of 24 sessions between T0 and T8 (three sessions per week). Non-adherence was assessed between T8 and T16. The dropout rate was calculated as the number of participants who terminated the training program and dropped out of the study.

2.7. Participant satisfaction

To evaluate participant satisfaction either with the training program or the stretching protocol, participants were asked at the end of the final biomechanical assessment (T8) to complete a questionnaire using a 5-point Likert scoring scale with the affirmatives: “I am satisfied with the exercising protocol (or stretching protocol, for the CG)”; “The exercising protocol is easy to perform (or stretching protocol, for the CG)”; “The exercising protocol is fun to perform (or stretching protocol, for the CG)”; “The exercising protocol reached my expectations (or stretching protocol, for the CG)”;

“The exercising protocol improved somehow my running practice (or stretching protocol, for the CG)”. Responses were completed anonymously.

2.8. Effect of the intervention

The effect of the intervention was assessed by measuring foot isometric strength, the intrinsic foot muscle's anatomical cross- sectional area (ACSA) and foot biomechanics during running. Foot isometric strength was measured using a pressure platform (EMED, Novel, Munich, Germany), which according to (Mickle, Chambers, Steele, & Munro, 2008), is a reliable way to assess foot muscle strength demonstrated by the intraclass correlations between assessment sessions (ICC(2,3) > 0.92). For this purpose, the subjects, while standing, pushed down on the platform as hard as possible with their hallux and toes, which control for excessive body sway. The peak force under the hallux and toes normalized by bodyweight were the outcomes of this measurement.

ACSA of the abductor hallucis, abductor digiti minimi, flexor hallux brevis and flexor digitorum brevis were measured using magnetic resonance imaging (MRI) and a protocol described by Matias et al. (2016). ACSA for each muscle was determined for each slice in which that muscle was visible according to Miller et al. (2014), using ImageJ software (Fig. 3). For the muscle cross- sectional area, it is reasonable to expect changes similar to the ones found by Jung et al. (Jung et al., 2011) or Ridge et al. (Ridge et al., 2018), since both studies' interventions were based on foot exercises, which resulted in an average of 11.18% and 11.32% muscle size growth respectively.

Finally, foot kinematics during overground running was obtained while subjects ran at a comfortable pace along a 14-m walkway in a biomechanics laboratory. Foot kinematics was acquired by 3D displacements of passive reflective markers tracked by eight infrared cameras at 200 Hz (Vicon® VERO, Vicon Motion System Ltd., Oxford Metrics, UK). Fourteen reflexive-passive markers (9 mm diameter) were placed on each subject's foot according to the Institute Orthopaedic Rizzoli Foot Model (IOR Foot Model) (Leardini et al., 2007; Portinaro, Leardini, Panou, Monzani, & Caravaggi, 2014). Kinematic data was processed using a zero- lag, second-order, low-pass filter with cutoff frequency of 12 Hz. We calculated the range of motion in the frontal and sagittal planes: second metatarsal to the fifth, second metatarsal to the first, fifth metatarsal to the ground, second metatarsal to the ground, first metatarsal to the ground and medial longitudinal arch. A limitation of the present study is that the assessment of the runners was in a controlled laboratory and not in their running environment and wearing of shoes during their regular practice, however it would be very difficult to perform the same biomechanical assessment under these real-life conditions.

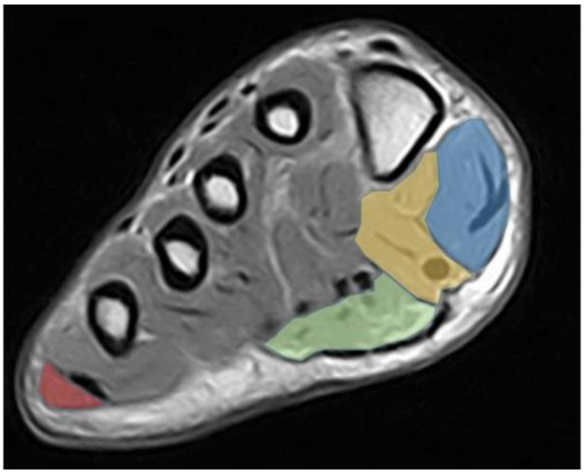

Figure 3. Example of a MRI slice and the four muscles of interest circumscribed. Abductor digiti minimi (in red), flexor digitorum brevis (in green), flexor hallucis brevis (in yellow) and abductor hallucis (in blue).

2.9. Statistical analysis

An a-priori power calculation (a 0.05, b 0.80) was performed on the incidence of running-related lower-limb injuries (Matias et al., 2016) using an effect size between the intervention group and control group of 0.28, a chi-square (chi-squared test) as a statistical design and contingency tables (df 1), and a dropout rate of 10%. This resulted in 112 participants who had to be randomized to detect a moderate effect in primary outcome. This effect size used was based on Taunton's et al. study (Taunton et al., 2003), and we took into account the proportion between the 236 injuries in the lower limbs found in 844 total participants (effect size=0.28).

To avoid undersampling, after 16-weeks, we conducted a post hoc power analysis on the parameters foot strength, muscle ACSA and running kinematics to estimate accurately if further analysis at trial completion would maintain enough statistical power (80%) for the variables, given the number of subjects included. We used the results obtained in this feasibility study and the effect sizes (Morris & Morris, 2010) retrieved from the data gathered so far. Sample sizes were calculated using G*Power software (v.3.1.9.2) (Faul, Erdfelder, Lang, & Buchner, 2007), and we included the following parameters in the analysis: F-tests family, ANOVA repeated measures, within-between interaction, power of 0.80 and a 0.05.

Two-way ANOVAs(2X2) were performed using the software Statistica™(V.10), comparing muscle strength and ACSA of both groups at T0 and T8 for effect of training assessment.

Table 1. Mean and standard deviation of participants' characteristics from the Control Group and Intervention Group.

	Control Group (n=15)	Intervention Group (n=16)
Age (years)	44.8 (8.7)	39.4 (8.5)
Height (cm)	168.7 (8.8)	169.6 (9.4)
Gender	M = 7F = 8	M = 11 F = 5
Body Mass (kg)	67.8 (12.7)	70.7 (12.4)
Arch Index (Cavanagh & Rogers) (Cavanagh & Rodgers, 1987)[37]	R = 0.25 (0.22) L = 0.18 (0.09)	R = 0.22 (0.19) L = 0.23 (0.16)
Training volume (km)	34.07 (13.58)	33.50 (20.99)
Average Pace (min/km)	5.97 (1.03)	6.46 (1.47)
Previous running-related injury more than 3 months before the beginning of the study (%)	53.3%	56.2%

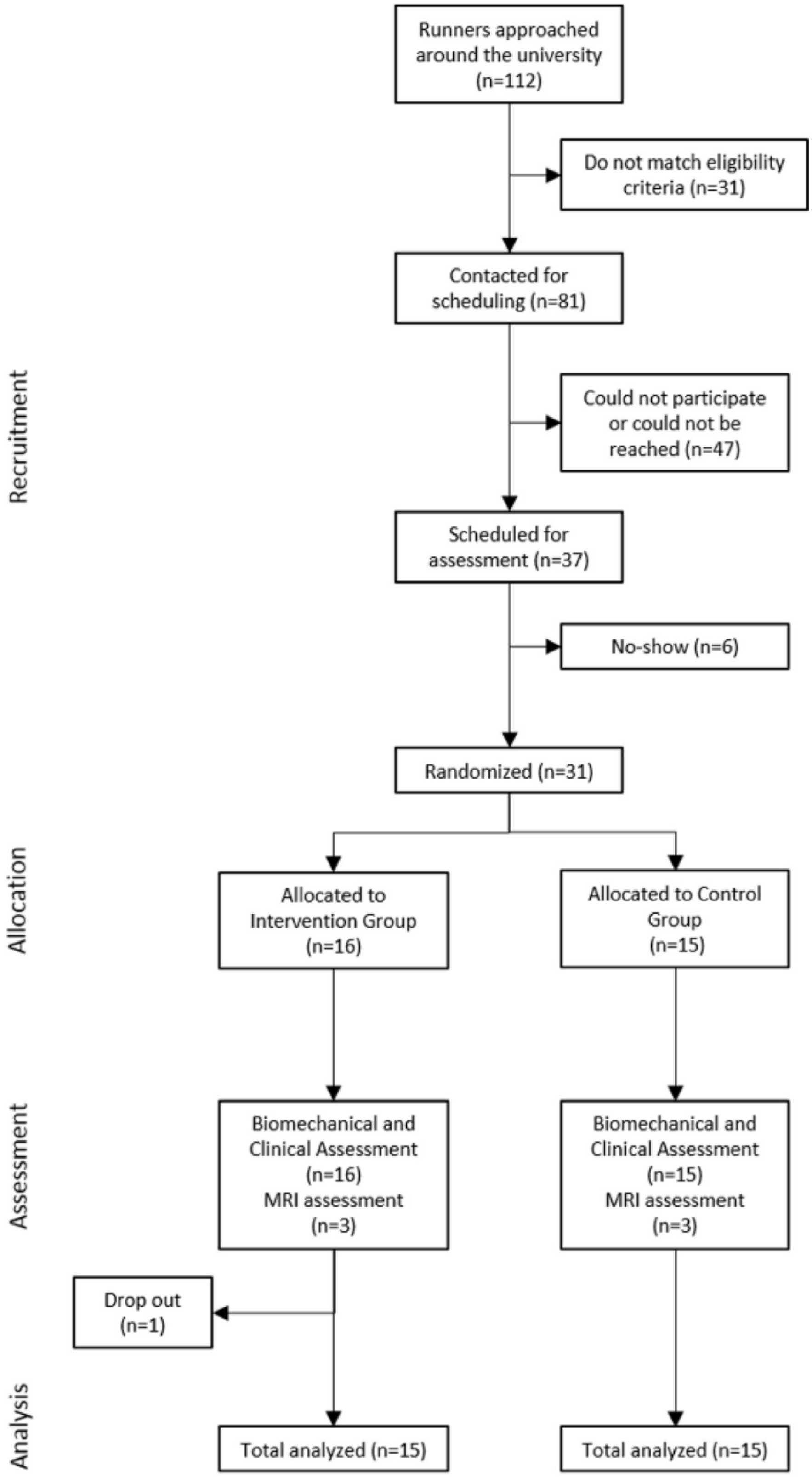

Figure 4. Flow chart with runners' participation in the feasibility study.

3. Results

3.1. Recruitment

In the first two weeks of recruitment through digital advertisement and direct contact with runners and coaches, the total number of subjects initially eligible was 112 long-distance runners (69 males, 43 females). This means that 112 runners were willing to participate after being informed about the study. Of these 112 runners, 31 (27.7%) did not match the eligibility criteria, resulting in a recruitment rate of 40.5 subjects/week.

Each block of assessment (T0, T8, T16) consisted of two consecutive weeks of measurements, and each block was four- weeks apart. We scheduled approximately nine runners each week of assessment (4 non-consecutive weeks of assessment). For this feasibility study, 37 runners were scheduled for assessment and 31 were effectively measured at T0, T8 and T16 in 7 months' time (Fig. 4, Table 1). Of these 31 subjects, 16 were randomly assigned to the intervention group and 15 to the control group.

Recruitment success was 28% (31 runners successfully assessed out of 112 initially eligible runners). Recruitment success was mostly determined by fulfilling the eligibility criteria, the period that the biomechanics laboratory facilities were operational, the time spent on each biomechanical assessment and the strategy to avoid scheduling follow-up assessments in the same week as the baseline assessments were scheduled.

It was possible to assess only 20 runners a week due to the availability of the lab and research personnel. Thus, accounting for the possible need to reschedule subjects, two consecutive weeks were booked for baseline assessments: the first week with an overbooking of 16% (a measured rescheduling rate) and a second week initially with no scheduled assessments. Therefore, it resulted in 24 runners scheduled during each of the two weeks. Baseline assessment takes about 1 h and 45 min to perform and the subsequent biomechanical assessment takes 40 min, limiting the number of daily assessments from 4 up to 6. However, most runners are only available before 9 a.m. and after 5 p.m.

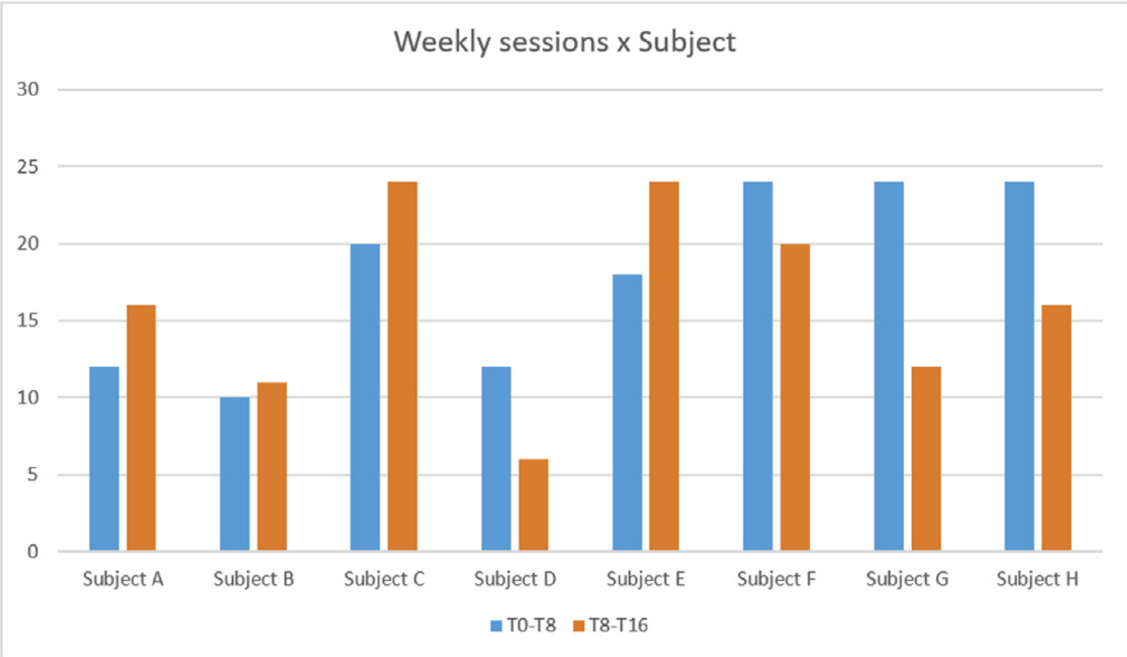

Figure 5. Number of foot exercise sessions performed by the subjects who did not complete the minimum expected of 24 sessions between T0 and T8 and between T8 and T16.

The number of subjects contacted and scheduled out of the total screened in a fixed period was deemed a “successful recruitment rate” and it is a better predictor of how many runners have to be approached in order to include the desired number of subjects. Based on the recruitment success rate of 28%, 405 runners are needed as initially available subjects to achieve the 112 included runners for the RCT with running-related injury as the primary outcome.

3.2. Adherence to the training program

Five of the 16 subjects (31%) of the intervention group did not complete all 24 sessions required between T0 to T8 (subjects A to E in Fig. 5). Six of the 16 subjects from the intervention group did not complete all required sessions between T8 and T16 (38%) (subjects A,B,D,F,G and H in Fig. 5). Four subjects performed more than the 24 sessions required (25%).

The average adherence rate was 87% between T0 and T8, while adherence between T8 and T16 was 83%. One out of 31 participants withdrew from the study, resulting in a 3% dropout rate. Four runners were absent for their scheduled biomechanical assessment at T8 (87% attendance) and five were absent for the assessment at T16 (83% attendance): two absences were due to a running-related injury; two absences were due to a non-running related injury; one dropout and one absence were due to the long travel distance.

Some of the challenges faced during the locally supervised training were reaching a common period for group training during business hours, rescheduling absent subjects for different reasons (mostly related to their work habits or travel across the city of São Paulo).

3.3. Participant satisfaction

Satisfaction with the therapeutic foot-ankle exercise program and with the stretching protocol were very similar (Fig. 6), and after a Mann-Whitney test, the only significant difference was found in statement 4 about the protocol satisfying the subjects' expectations (P=0.018), with lower scores for the foot exercise protocol.

Participants were questioned on what would make them practice the foot exercise protocol more often and they answered that more information about the purpose of each exercise and the possible benefits would do so.

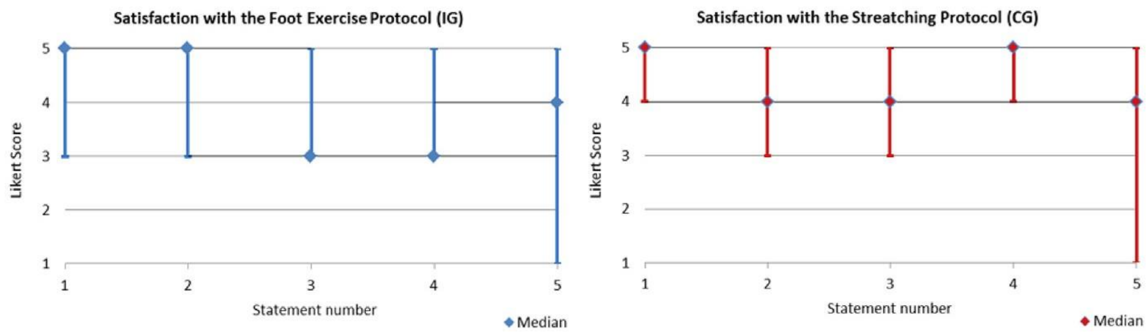

Figure 6. Median, maximum and minimum scores of the Likert scale on the 5 statements answered by the runners at the end of T8 about the foot exercise protocol (IG) (left) or about the stretching protocol (CG) (right).

Table 2. Strength of Hallux and Toes show as percentage of bodyweight measured by pressure platform at baseline (T0) and at eight weeks (T8) for the control group and intervention group. P-values reported from the interaction effect of two-way ANOVAs (2x2) repeated measures, standard error of mean (SEM) reported in percentage of bodyweight.

Foot Region		T0	T8	T8-T0	% of the difference	SEM	p-value
Right Hallux	control	11.70 (6.90)	12.83 (5.25)	1.13	9.6%	1.01	0.314
	intervention	10.33 (4.44)	13.37 (6.59)	3.04	29.4%	0.92	
Right Toes	control	10.23 (9.05)	9.13 (4.18)	—1.10	11%	1.10	0.675
	intervention	8.18 (3.98)	9.17 (3.47)	0.99	12.1%	0.62	
Left Hallux	control	11.34 (5.52)	12.86 (5.66)	1.52	13.4%	0.93	0.134
	intervention	8.28 (3.72)	11.29 (3.72)	3.01	36.3%	0.62	
Left Toes	control	7.14 (3.52)	7.87 (3.66)	0.73	10.2%	0.59	0.183
	intervention	7.60 (3.64)	9.58 (4.29)	1.98	26.0%	0.67	

3.4. Effect of the intervention

The two-way ANOVA (2 2) did not reveal a significant differ- ence in the intervention group on the strength of the hallux and toes after eight weeks (Table 2), even though peak values seem higher for the intervention group.

There was a significant increase in ACSA for the abductor hallux (P=0.040) and flexor digitorum brevis muscles (P=0.045) with an interaction effect (evaluation x group), showing a strengthening effect of the training protocol on these muscles in the intervention group. This effect might be due to initial differences between groups, however further detailed analysis are needed to check the impact of these eventual differences between groups at baseline, when the full sample size is gathered. Effect sizes were calculated according to Morris & Morris (2010) for the ASCA of each muscle of interest and are shown in Table 3.

Table 3. Anatomical Cross-sectional area (mm2) of the intrinsic foot muscles of interest at T0, T8, effect sizes and two-way ANOVA's (2 × 2) p marked with * when significantly different.

ACSA		T0 (mean ± SD)	T8 (mean ± SD)	Effect Size (f)	SEM (mm^2)	T8-T0	% of difference	p-values (ANOVA)
Abductor Hallucis	control	208.0±62.7	191.2±70.4	0.34	13.3	—16.8	8.%	0.040*
	intervention	178.9±36.4	201.1±57.5		9.3	22.2	12.4%	
Abductor Digiti Minimi	control	115.2±28.9	111.6±29.7	0.23	5.8	—3.6	3.1%	0.400
	intervention	130.7±22.1	140.4±19.5		4.1	9.7	7.4%	
Flexor Hallucis Brevis	control	239.3±47.2	145.2±98.1	0.02	14.5	—94.1	39.3%	0.844
	intervention	237.7±20.0	236.4±42.2		6.2		0.5%	
Flexor Digitorum Brevis	control	146.0±77.1	139.9±81.8	0.29	16.9	—6.1	4.1%	0.045*
	intervention	136.8±7.6	165.8±18.1		2.6	29.0	21.2%	

Figs. 7 and 9 show the outcomes of foot kinematics. A high degree of inter-subject variability was present in the kinematic parameters. Some differences in patterns in the joint range of motion in the second metatarsal to the fifth metatarsal bone (S2V) and fifth metatarsal to the ground (V2G) were present between groups for each biomechanical assessment (T0, T8 and T16).

3.5. Power analysis on the available data

Sample sizes recalculated for 10 out of 12 variables remained below the previous calculated 112 subjects that are necessary for the clinical trial on running-related injury, except for the ACSA of the flexor digitorum brevis muscle and one foot kinematic variable, due to the small effect sizes found for these parameters (f ¼ 0.02 and f ¼ 0.03, respectively) (Table 4).

Table 4. Effect size (f) and resulting sample size recalculation for 0.80 statistical power of the Abductor Hallucis (ABH), Abductor Digiti Minimi (ABV), Flexor Hallucis Brevis (FHB) and Flexor Digitorum Brevis (FDB) cross-sectional area (ACSA); hallux and toes strength, and range of motion of the fifth metatarsal to the ground, second metatarsal to the ground, first metatarsal to the ground, second metatarsal to the first, second metatarsal to the fifth and medial longitudinal arch during running.

	Effect size (f)	Sample size required for a power 80%
ACSA Muscle ABH	0.34	20
ACSA Muscle ABV	0.23	40
ACSA Muscle FHB	0.02	4906
ACSA Muscle FDB	0.29	26
Hallux strength	0.17	70
Toes Strength	0.16	80
Fifth metatarsal to the ground	0.24	38
Second metatarsal to the ground	0.15	86
First metatarsal to the ground	0.19	58
Second metatarsal to the first	0.03	2184
Second metatarsal to the fifth	0.25	34
Medial longitudinal arch	0.97	6

4. Discussion

Feasibility studies play a critical role as an essential preliminary step for assessing the effect of an intervention in a complex RCT (Craig et al., 2013; Ribeiro, Sole, Abbott, & Milosavljevic, 2014), such as the one we are conducting involving a therapeutic foot exercise program applied to long-distance runners focused on improving foot structure, strength and biomechanics, and, eventually, the prevention of injury (Matias et al., 2016).

The recruitment rate was satisfactory (40.5 runners/week), and it was mostly determined by the time the biomechanics laboratory was operational, time spent on each biomechanical assessment and some challenges in finding runners who matched the eligibility criteria. Because only 28% of the eligible subjects were assessed (recruitment success), one of the challenges is to enlarge the list of potential runners to increase the chance of finding a runner who matches all the eligibility criteria. Other forms of advertisement are now adopted (for instance, Facebook leads) to increase the recruitment rate and success.

One of the challenges in the recruitment was the difficulty in scheduling biomechanical assessment and MRI exams during business hours, and this resulted in overscheduling in the early mornings and late afternoons. The recruitment of runners and their assessment had to be carried out at no more than one month apart at most, to avoid loss of interest and an increase in no-shows for the first assessment.

The participants' satisfaction with the training program was high for both groups, and we observed similarities in the runners' opinions about both interventions, which is positive because it diminishes the chance of eventual differences due to the nocebo effect (Haüser, Hansen, & Enck, 2012).

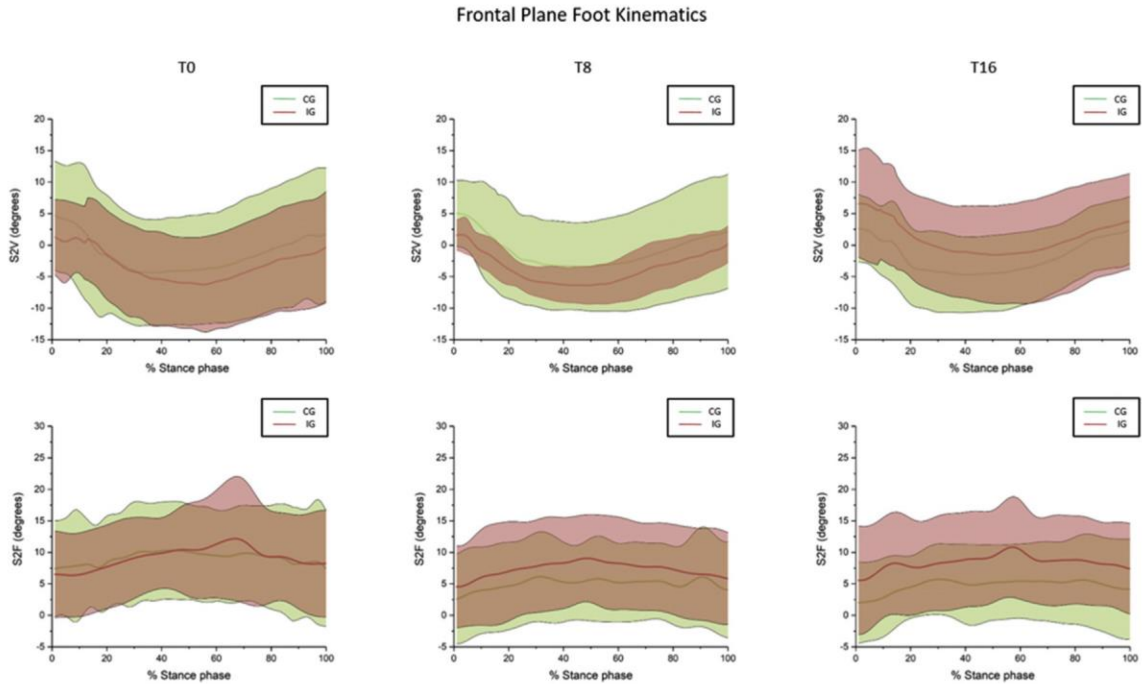

Figure 7. Mean and standard deviation of the time series of the foot kinematics in frontal plane during running in T0, T8 and T16 for the control group (CG) and the intervention group (IG), represented by the range of motion of the second metatarsal to the fifth (S2F).

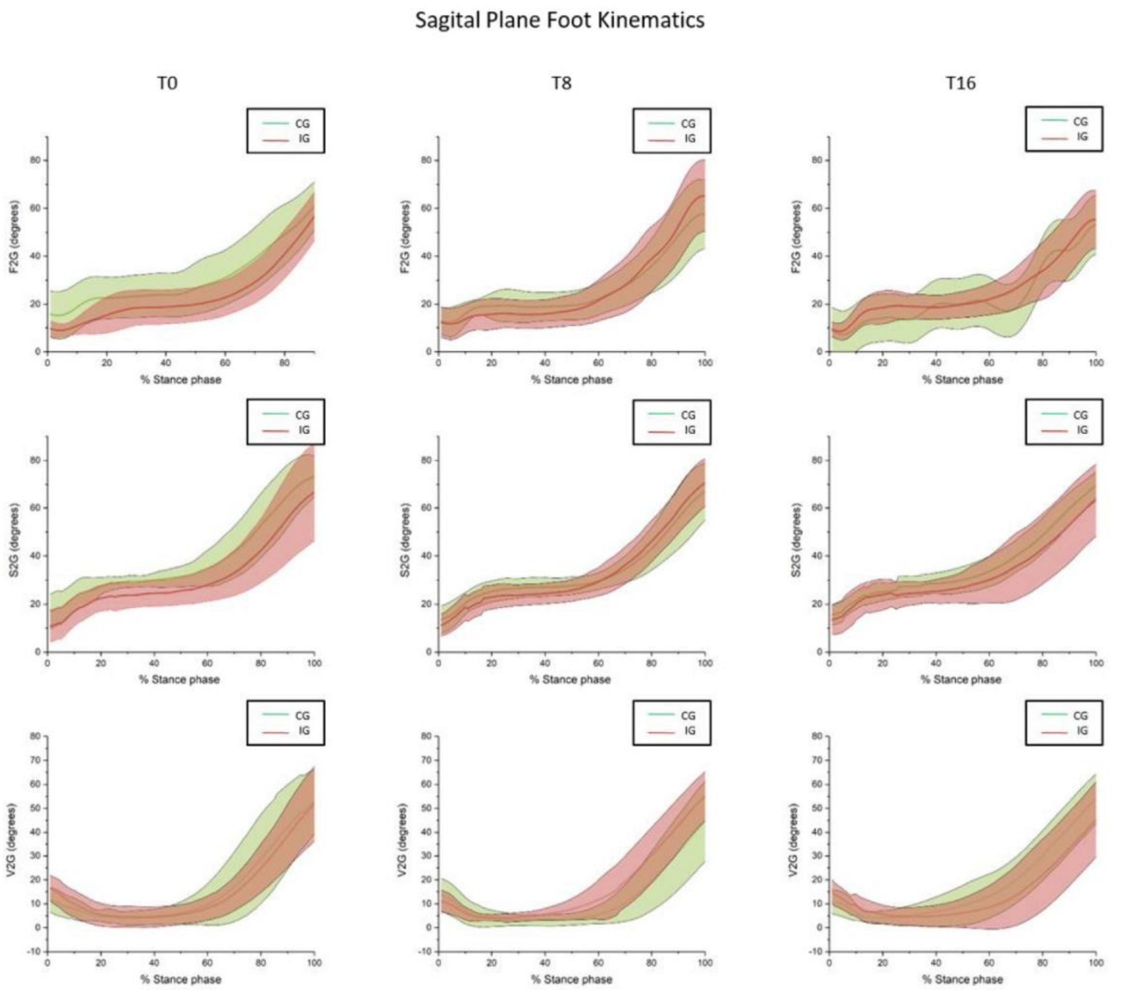

Figure. 8. Mean and standard deviation of the time series of the foot kinematics in sagittal plane during running in T0, T8 and T16 for the control group (CG) and the intervention group (IG), represented by the range of motion of the first metatarsal to the ground (F2G), second metatarsal to the ground (S2G), the fifth metatarsal to the ground (V2G).

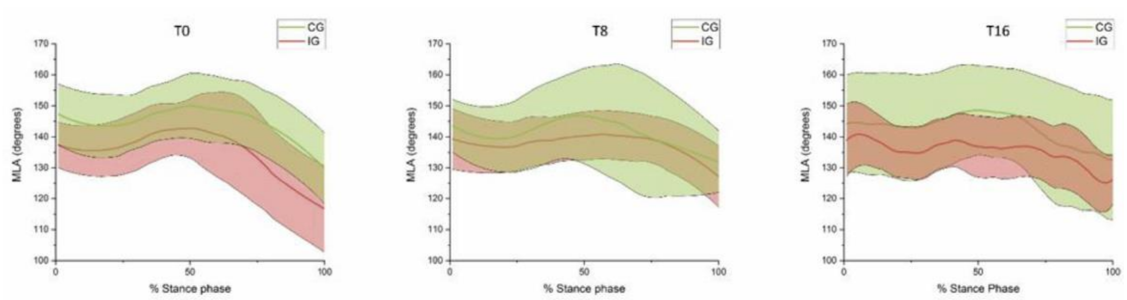

Figure. 9. Mean and standard deviation of the time series of the foot kinematics in sagital plane during running in T0, T8 and T16 for the control group (CG) and the intervention group (IG), represented by the range of motion of the medial longitudinal arch (MLA).

To date in the trial, only 14 of the 31 subjects completed the full 12-month follow-up, but the dropout rate was a very low 3%; the subject who withdrew from the running practice cited lack of time as the reason. Both the adherence rate between T0 and T8 and between T8 and T16 were above 80%, which was the threshold adopted in this feasibility study to be considered a successful adherence (“Oxford Centre for Evidence-based Medicine - Levels of Evidence (March 2009) - CEBM,” n.d.). Baltich, Emery, Whittaker, & Nigg (2017) found that only 51% of the intervention group completed the four weekly sessions required. Johnen and Schott (Johnen & Schott, 2018) reported a lower adherence - 87.5% in strength training in an elderly population. Runners reported that additional knowledge regarding the effects of each exercise would further enhance their adherence to the protocol. This matches the results obtained by Keukenkamp, Merkx, Busch-Westbroek, & Bus (2018), who explored the efficacy of informing diabetic patients on the importance of the proper use of custom footwear on footwear adherence. This information being part of a “motivational inter-viewing” intervention improved footwear adherence right after baseline but not at the 3-month follow-up.

The training protocol showed a significant effect on the ACSA of the abductor halluces and flexor digitorum brevis muscles, and signs of improvement on the abductor digiti minimi muscle, but not for the flexor hallux brevis. Muscles whose origin and insertion matches the beginning and the end of the foot longitudinal arch are probably more prone to the effect of training exercises that target the arch. Since the abductor hallucis, flexor digitorum brevis and abductor digiti minimi have a greater lever arm than the flexor digitorum brevis, a small change in the arches put them easily at tension, such as the longer cables on an extradosed bridge (Fig. 10). Foot muscle strength measured by a pressure platform did not show any effect of the intervention. In the sample size recalculation, we found that we need at least 46 subjects to draw a relevant conclusion about this parameter. Regarding foot kinematics, we observed changes in two out of six parameters in the intervention group compared with the control group, although the variability is very high and probably a greater sample size is needed for any relevant conclusion.

Figure. 10. Different tensions on the foot muscles according to origin and insertion (left). White arrow representing the tension on the Flexor Digitorum Brevis and yellow arrow representing the tension on the Abductor Hallucis due to the same arch strain. To the right, the Matakina extradosed bridge in Japan, to which a torque would tend to enhance the tension on the red longer cables. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

As a final assessment for feasibility, a post hoc power analysis was performed using the effect sizes between groups on selected parameters to ascertain if the a priori calculated 112 subjects for the trial with running-related injury as a primary outcome would be enough for the other variables to keep a 0.80 statistical power. For intrinsic foot muscle ACSA, the sample size considered feasible was 40, which is slightly higher than the number of MRIs previously planned (one-third of the total sample size resulting in 38) (Matias et al., 2016). We have now set the goal at 50 subjects to be assessed by MRI (at T0, T8 and T16) to assess the effectiveness of the intervention on intrinsic foot muscle ACSA at the full trial. It will require a minimum of 80 subjects as a sample for hallux and toes flexion strength, which will be reached by the completion of the study. From the kinematic data, the variation of temporal series was quite substantial, probably because in a first analysis, forefoot and rear- foot strikers were analyzed together. For foot range of motion, effect sizes ranged from small (S2G) to great (MLA), although recalculation of the sample size did not exceed the 112 previously calculated for most of the variables, with the exception of range of motion of the second metatarsal to the first, which achieved a sample size of 2184. Particularly, this former variable and the ACSA of FHB showed a small effect size, thus, a new sample size calculation would be performed after assessing 112 runners to answer whether the protocol is not effective on changing these variables or if the operational variable is inadequate to investigate the phenomenon.

In summary, we conclude that this RCT on the effects of a therapeutic foot exercise program on injury incidence, foot functionality and biomechanics in long-distance runners is feasible, given an accessible study population that is willing to participate, perceives the training program as positive and adheres to the program. The training intervention did enhance the ACSA of the longer intrinsic foot muscles, which justifies assessing clinical outcomes in this RCT.

Trial registration

Clinicaltrials.gov Identifier NCT02306148 (November 28, 2014) under the name "Effects of Foot Strengthening on the Prevalence of Injuries in Long Distance Runners." Committee of Ethics in Research of the School of Medicine of the University of São Paulo (18/03/2015, Protocol no. 031/15).

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5. PUBLISHED PAPER 2

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Original Research

Effects of a foot strengthening program on foot muscle morphology and running mechanics: A proof-of-concept, single-blind randomized controlled trial

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abstract

Objectives: To investigate the effects of a foot training program on muscle morphology and strength as well as running biomechanics in healthy recreational runners. Design: Proof-of-concept, single-blind randomized controlled trial.

Settings: Runners were allocated to a control (CG) or an intervention (IG) group. The intervention focused on strengthening the intrinsic foot muscles and their activation during weight-bearing activities. All participants were assessed at baseline and after 8-weeks.
Participants: Twenty-eight healthy recreational long-distance runners not habituated to minimalist running shoes or barefoot running.
Main outcomes measures: Outcomes were hallux and toes strength; foot function, cross-sectional area and volume of the abductor hallucis (ABH), abductor digiti minimi (ABV), flexor digitorum brevis (FDB), and flexor hallucis brevis; medial longitudinal arch range of motion and stiffness; vertical and antero-posterior propulsive impulses during running.

Results: Compared to the CG, an increase was found in the IG for the volume of all muscles investigated and for vertical propulsive impulse during running. Correlations were found between vertical propulsive impulse and volume of ABH(r ¼ 0.40), ABV(r ¼ 0.41), and FDB(r ¼ 0.69).
Conclusion: The foot exercise protocol effectively increased intrinsic foot muscle volume and propulsive forces in recreational runners. This shows that intrinsic muscle strengthening affects running mechanics and suggests that it may improve running performance.

1. Introduction

The complex structure of the foot includes 26 bones, 20 intrinsic and 9 extrinsic muscles, 108 ligaments, and more than 30 joints, which all act in unison and play an important role in bipedal locomotion(Hillstrom et al., 2013; Holowka & Lieberman, 2018; Lieberman et al., 2015; Mckeon, Hertel, Bramble, & Davis, 2014). During high-intensity sports activities such as running, the foot not only needs to be compliant to assist in ground reaction force attenuation, it also be able to resist deformation and provide a stable base of support and lever arm to propel the body efficiently (Bramble & Lieberman, 2004; Luke A.; Kelly, Kuitunen, Racinais, & Cresswell, 2012; Mckeon et al., 2014). A foot that is unable to adjust to these stresses may alter resultant moments and forces acting on the more proximal joints (Buldt et al., 2015; Sawada et al., 2017, 2016), possibly leading to overuse injuries throughout the lower extremities (Mei, Gu, Xiang, Baker, & Fernandez, 2019; Son, Kim, Seeley, & Hopkins, 2019; Teng, Kong, & Leong, 2017).

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Introduction

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In a healthy foot, the intrinsic muscles play an important role in maintaining the foot arches; absorbing, dissipating, and returning kinetic energy during running; and generating power and torque (Fukano & Fukubayashi, 2009; Ker, Bennett, Bibby, Kester, & Alexander, 1987). Evidence shows that when these intrinsic foot muscles are weak or dysfunctional, these roles are compromised (Miller, Whitcome, Lieberman, Norton, & Dyer, 2014; Nigg, 2009), increasing loads on other foot passive structures, promoting excessive pronation, compromising performance, and increasing the incidence of foot deformities (Kaufman, Brodine, Shaffer, Johnson, & Cullison, 1999; Mickle, Munro, Lord, Menz, & Steele, 2009; Miller et al., 2014) and injuries.

There is evidence, though, that simple foot interventions, even in healthy young subjects, are enough to change foot deformities, and improve performance. Kim et al. (Kim et al., 2015) studied the effects of different treatment approaches on individuals (19 to 29 yrs old) with hallux valgus. The participants were divided in two groups: one receiving only foot orthosis and the second, receiving additionally to the orthosis, a foot training that included a toe spreading exercise 20 min/day, 4 days/week. The study showed superiority of the training group, where individuals had increased the abductor hallucis cross-sectional area and reduced significantly the hallux valgus angle. Regarding the enhancement in sport performance, Unger and Wooden (Unger & Wooden, 2000) observed a positive effect on vertical and horizontal jumping performance after 6 weeks of a toe flexor strengthening in healthy physically active subjects. Similarly, Goldmann et al. (Goldmann, Sanno, Willwacher, Heinrich, & Brüggemann, 2012) also observed an increased performance in the jump performance after 7 weeks of toe flexor muscle training in healthy males.

The seminal paper by Robbins and Hanna (Robbins & Hanna, 1987) showed that merely encouraging healthy subjects to perform weight bearing activities at home and outdoors as much as possible without wearing any footwear resulted in an increased arch height.

Although few physical therapy programs for muscle strengthening include foot-specific strengthening strategies, studies on training the intrinsic and extrinsic foot muscles have shown promising results. Mulligan and Cook (Mulligan & Cook, 2013) found that strengthening the foot muscles using a single at-home foot exercise daily for 4 weeks lowered the navicular drop by an average 14%. Lynn, Padilla, and Tsang(Lynn, Padilla, & Tsang, 2012) compared two different exercises (towel curl and short foot) in two groups of healthy subjects and showed that after a 4-week period, the center of pressure displacement during the star excursion test decreased in both groups, indicating the positive effect of foot muscle strength on functional balance tasks. Mickle et al. (Mickle, Caputi, Potter, & Steele, 2016) were able to improve hallux and lesser toe strength, single leg balance, and general foot health of subjects aged between 60 and 90 years using a customized progressive Toe Training exercise program, showing that even elderly people benefit from foot training. The program developed was taught in 45-minutes weekly sessions over 12 weeks.

These findings led to the question of how changes in muscle strength affect running. Knowing the role of the intrinsic foot muscles in storing and returning energy(Luke A Kelly, Cresswell, & Farris, 2018; Ker et al., 1987), stiffening the foot arches during running,(L A Kelly, Lichtwark, & Cresswell, 2015) and being a sensorial organ(Mckeon et al., 2014), it is expected that strengthening the intrinsic muscles will improve running mechanics and performance as well as prevent injury due to impact overload, accumulated load, or fatigue. Thus, this study seeks to verify if these changes to the foot's arch, structure, and functional balance are linked to the strength gain from intervention protocols.

It is expected that improvement in foot muscle morphology and strength would lead to increased foot stiffness, (Holowka & Lieberman, 2018) and that the effects of a stronger foot can be measured by improved force transmission through the foot to the ground during running. Kelly et al. (L A Kelly et al., 2015) showed that the abductor hallucis (ABH), flexor digitorum brevis (FDB), and quadratus plantae muscles had higher activation during late stance in walking and running on an instrumented treadmill. This higher activation facilitates effective foot ground force transmission, enabling higher ground reaction forces to be transmitted over a shorter period of time. Thus, the aim of this proof-of-concept, single-blind randomized controlled trial was to investigate the effects of a foot muscle strengthening and training program on foot function, intrinsic foot muscles morphology and strength, as well as running biomechanics in healthy recreational runners. We hypothesized that the training program would improve intrinsic foot muscle volume, isometric strength of the toes and hallux, propulsive forces while running, and medial longitudinal arch (MLA) mechanics.

Methods

Design

The study was a single-blind, proof-of-concept randomized controlled trial with two study arms.

Subjects

Twenty-eight recreational long-distance runners (Table 1) were recruited through online advertisements (Laboratory of Biomechanics website, www.usp.br/labimph) and by directly approaching running clubs located around the university campus. Participants were eligible if they ran at least 20 km but no more than 100 km per week, were between 18 and 55 years of age, and had no lower limb injury or pain in the 3 months prior to baseline assessment. Participants were excluded if they were under any physical therapy treatment at baseline, had a history of using minimalist shoes or barefoot running, presented with any orthopedic or neurologic impairment or major vascular complication, had previous lower-limb surgery, or had diabetes mellitus. All participants were assessed at baseline (T0) and after 8 weeks (T8) of the foot exercises program. After T0, participants were randomly allocated in blocks based on numbers generated by the random allocation program ClinStat (University of York, Heslington, UK)(Bland, 2015). The code for each group was kept in opaque and sealed envelopes, and an independent researcher assigned the participants to either the control group (CG) or intervention group (IG). Only the physiotherapist responsible for the intervention knew who was receiving it. Blinded examiners performed all the assessments. The trial statistician was blind to treatment allocation until the main analysis has been completed. All participants' data was kept confidential before, during, and after the study by encoding their names.

This study was part of a larger trial approved by the Research and Ethics Committee of the School of Medicine of the University of São Paulo (18/03/2015, Protocol no. 031/15) and registered with ClinicalTrials.gov (Identifier NCT02306148 November 28, 2014). All runners consented to participation after receiving information on all details of the study.

Table 1- Mean and standard deviation of participants' characteristics from the control group (CG) and intervention group (IG) at baseline.

	CG (n = 14)	IG (n = 14)	p-value
Age (years)	41.6 ± 6.0	41.9 ± 7.4	0.890[a]
Height (cm)	169.40 ± 9.18	166.40 ± 7.80	0.113[a]
Sex	Male: 9; Female: 5	Male: 5, Female: 9	0.131[b]
Body mass (kg)	75.1 ± 13.9	68.3 ± 12.7	0.110[a]
Running experience (years)	10.9 ± 7.9	6.2 ± 6.3	0.095[a]
Running volume (km)	30.8 ± 13.4	28.5 ± 9.5	0.639[a]
Average pace (min/km)	6.4 ± 1.3	6.4 ± 0.9	0.843[a]
Foot posture index (median, min:max) (Redmond, Crane, & Menz, 2008)	Right: 2,4:9 Left: 2.5,3:8	Right: 1.5,6:10 Left: 2.5,6:10	0.369[a]
Arch index (Cavanagh & Rodgers, 1987)	Right: 0.23 ± 0.16 Left: 0.16 ± 0.03	Right: 0.22 ± 0.10 Left: 0.16 ± 0.04	0.277[a]
Previous running-related injury more than 3 months before the beginning of the study (%)	21.4%	28.6%	0.225[b]

a p-values of t-tests.
b p-values of chi-square tests.

Intervention protocol

Participants in the IG performed an 8-week foot strengthening training with a physiotherapist once a week and at least three times at home over the entire course of the study. Participants reported their completed sessions and progress in an online software tool. Participants in the CG were instructed to perform an 8-week 5-minute warm-up and full body muscle stretching protocol before or after each running session. More details on the strengthening and stretching protocol are available in the published protocols for the trial (Matias et al., 2016). Adherence was monitored every locally supervised session and accounted as the number of sessions attended by the participants in the IG, where 100% of adherence would be a total of 112 completed sessions (14 subjects attending all 8 sessions).

Outcome measurements

For this proof-of-concept study, the main theoretical outcomes were related to the effectiveness of the intervention in improving foot function, foot muscle strength and foot biomechanics during running. These include hallux and toe isometric strength, intrinsic foot muscle anatomical cross-sectional area (ACSA) and volume, MLA range of motion (ROM) and stiffness, foot function scores, and propulsive impulses during running (vertical and antero-posterior).

Foot muscle isometric strength was measured using a pressure platform (EMED, Novel, Munich, Germany), which is a reliable way to measure foot muscle strength(Mickle, Chambers, Steele, & Munro, 2008). While standing with knees extended, participants pushed down as hard as possible using only their hallux and toes. During the assessment, the researcher checked whether the subject lifted the heel and inspected for fluctuations in the line of gravity and trunk posture during each trial. The runners were instructed to not curl their toes or grip the platform during the trial. Prior to the test, the runners were allowed to practice the movement to ensure comprehension of the task. If any changes were observed in the line of gravity or positioning of the heel or trunk, the trial was excluded. The outcome of the measurement was the peak force under the area of a mask, including the hallux and toes, normalized by bodyweight (BW) and reported as % BW.

The ASCA of the of the ABH, abductor digiti minimi (ADV), flexor hallucis brevis (FHB), and FDB were measured using magnetic resonance imaging of the right foot of each subject at T0 and T8 by the same technician following the protocol described by Matias et al. (Matias et al., 2016). ASCA was measured by a blinded researcher using ImageJ planimeter software (company, city, country) following the protocol by Miller et al.(Miller et al., 2014). Muscle volume was calculated by multiplying the sum of each ACSA measured for a specific muscle from each individual slice by the linear distance between slices (5 mm)(Miller et al., 2014).

Participants answered to the Foot Health Status Questionnaire (FHSQ)(Ferreira et al., 2008) at baseline and after 8-weeks and all eight domains were assessed: foot pain, function, shoe, general foot health, general health, physical activity, social capacity and vigor.

Foot biomechanics were assessed by having participants run barefoot on an instrumented treadmill (force plates at 1000 Hz) surrounded by eight infrared cameras (Vicon® VERO, Vicon Motion System Ltd., Oxford Metrics, UK; at 200 Hz) at a self-selected speed. The self-selected speed chosen at baseline was also used for assessment at T8. Foot kinematics were acquired based on 16 reflexive-passive markers (10 mm in diameter) placed on each subject’s foot according to the Rizzoli Orthopedics Institute Foot Model (Leardini et al., 2007; Portinaro, Leardini, Panou, Monzani, & Caravaggi, 2014). Based on residual analysis(Winter & Patla, 1997), kinematic and ground reaction force data were analyzed and processed using a zero-lag, fourth-order Butterworth filter and a low-pass filter with cutoff frequencies of 15 Hz and 100 Hz, respectively.

The outcomes chosen to represent the foot biomechanical responses to the exercise protocol were the ROM of the MLA during the stance phase of running and MLA stiffness during running. The MLA angle (Figure 1) was calculated as the angle formed by three reflective markers: at the upper central ridge of the calcaneus posterior surface, at the medial apex of the tuberosity of the navicular, and at the dorsomedial aspect of the first metatarsal-phalangeal joint, with the navicular tubercle as the MLA vertex.

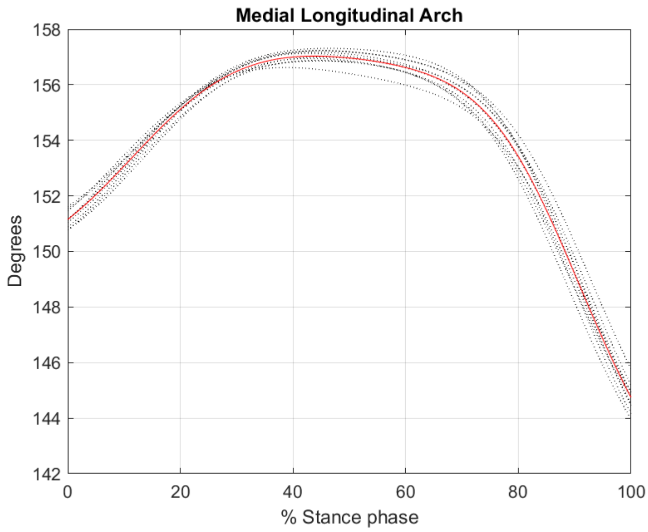

Figure 1. Temporal series of the MLA angle of 10 trials of a random participant (average in red) during running, normalized in time by the stance phase. The curve shows more obtuse angles of the arch during mid-stance.

MLA stiffness (kmid) was calculated according to Holowka, Wallace, and Lieberman(Holowka, Wallace, & Lieberman, 2018):

kmid= Fmid/ΔLAheight (1)

where Kmid is equal the vertical ground reaction force (VGRF) on the platform at 50% stance phase (Fmid) divided by the perpendicular distance between the navicular tuberosity marker to the line connecting the calcaneus marker to the first metatarsal head marker. Vertical impulse was calculated by integrating the VGRF curve over time from the propulsive peak to the end of stance phase (Running Impulse 1), corresponding to the push-off phase of running (Figure 2). The horizontal impulse of the accelerating phase was also calculated from the horizontal antero-posterior GRF (AP-GRF) (Figure 2), corresponding to the propulsive horizontal impulse (Running Impulse 2). The values in Newtons were then normalized for each participant's BW.

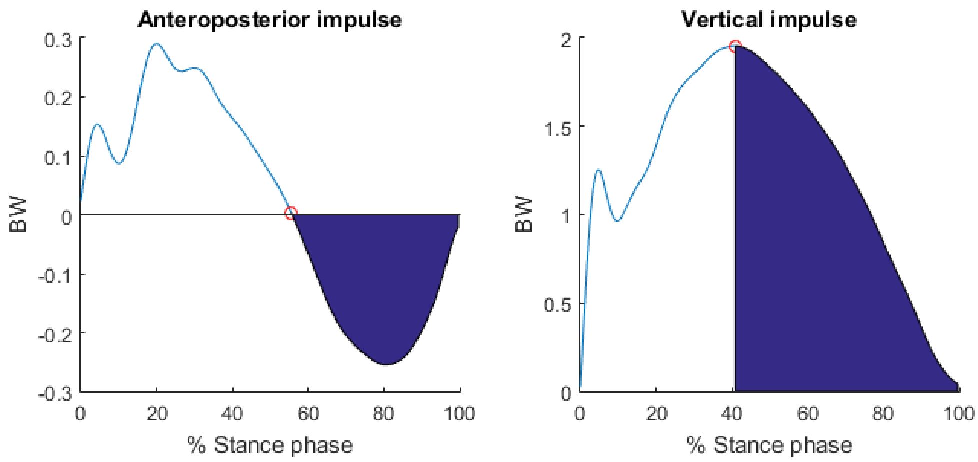

Figure 2. Anteroposterior and vertical impulses (normalized by BW) calculated from the ground reaction force time curve during stance phase while running on a treadmill.

Statistical analyses

Baseline characteristics of participants in the IG and CG were compared using two-tailed t-tests and chi-square statistics for continuous and discrete variables, respectively. A 2x2 repeated measures analysis of variance (ANOVA) was used to compare the interaction effect of training (foot strengthening vs. control) and time (T0 and T8) for the variables of each domain of the FHSQ, foot strength, muscle volume, muscle ACSA, MLA ROM, MLA stiffness, and impulses. In case of significant interaction effects, Tukey's HSD test was used to conduct pairwise comparisons to identify differences in time, group, or both. The minimal detectable change (MDC) for each variable was calculated according to Haley and Fragala-Pinkham (2006) as MDC = z-score (95% CI) × SEM × √2, in which the standard error of the mean (SEM) was obtained as follows SEM = SD × √(1 – ICC), where SD is the standard deviation and ICC is the intraclass correlation coefficient. Two-way mixed effects model ICC's were calculated using only the CG variables between T0 and T8. After that, each difference between T8 and T0 for the IG larger than the calculated MDC for the CG was accounted as an event and the event rates were compared between the two groups as relative risks (RR=absolute risk of event in the CG / absolute risk of event in the IG). The absolute risk (AR) was calculated as the number of events in the IG or CG, divided by the number of people in that group. In the case of no events of change in a variable greater than the MDC in one of the groups, only the AR was reported.

Pearson's product-moment correlations were performed to verify correlations between the studied variables at baseline (T0) for both groups together, as they started from similar baseline conditions, a joint analysis could bring results that are more robust with the larger, and no intervention was performed yet. Pearson's correlations were also performed for the IG using the differences (delta) between T8 and T0 for each dependent variable. This analysis allows verifying possible relations between changes after 8 weeks (positive or negative) with muscle morphology changes. Pearson's correlation coefficients were considered fair if between 0.3 and 0.5, moderate between 0.6 and 0.7, and strong between 0.8 and 0.9 (Akoglu, 2018). Cohen's d effect size was calculated for variables with significant differences between groups, and effects between 0.2 and 0.5 were considered small, between 0.5 and 0.8 were medium, and above 0.8 were large (Lakens, 2013).

Results

Foot strength measurements

There was no significant interaction effect between time (T0 and T8) and group (IG and CG) for Hallux and toe flexor isometric strength (CG: T0=23.46±4.86 %BW; T8=25.61±7.40 %BW; IG: T0=19.95±6.24 %BW; T8=27.31±9.33 %BW; p=0.707). At baseline, the groups were not different (p= 0.9362). Calculated MDC of 11.86 %BW resulted in a RR=0.31, meaning 69% reduction in relative risk for events in the CG with a non-significant confidence interval CI = [0.04-2.61].

Foot Function (FHSQ)

There were no differences at baseline between groups for any of the eight domains (p>0.05). There were also no significant effects of the intervention on the FHSQ score of any domain after eight weeks (p>0.05) (table 2).

Table 2 - Mean and standard deviation of the FHSQ domains scores. P-values of the interaction Group*Time for the Repeated measures ANOVAs considering significant p<0.05.

	CG (T0)	IG (T0)	CG (T8)	IG (T8)	p-value
Foot Pain	89 ± 16.1	92 ± 10.9	92 ± 12.6	93 ± 11.6	0.729
Foot Function	99 ± 2.3	100 ± 1.7	100 ± 0.0	100 ± 1.7	0.327
Shoe	82 ± 13.8	81 ± 27.5	78 ± 26.5	72 ± 35.6	0.683
General Foot Health	79 ± 22.1	83 ± 26.8	83 ± 27.6	92 ± 11.6	0.548
General Health	81 ± 20.2	86 ± 10.4	90 ± 9.13	87 ± 13.8	0.184
Physical Activity	92 ± 26.6	99 ± 2.1	99 ± 2.1	100 ± 1.5	0.327
Social Capacity	91 ± 13.4	91 ± 12.9	94 ± 9.7	93 ± 10.9	0.753
Vigor	83 ± 11.1	80 ± 9.8	76 ± 10.8	78 ± 7.9	0.366

Intrinsic foot muscle size

There was a significant increase in the volume of all measured muscles after 8 weeks of training for the IG compared to the CG (interaction effects Time x Group for ABH: p=0.019; ABV p=0.013; FDB p=0.039; FHB p=0.009). In the IG, there was a 22.3%

increase after the intervention compared to baseline for ABH, 12.1% for ABV, 8.8% for FDB, and 17.7% for FHB. At baseline, there were no differences between the groups regarding muscle size ($p>0.05$), with the exception of the FDB muscle volume ($p=0.028$). Values in cm^3 and Cohen's d effect sizes are reported in Table 3. The MDCs obtained were 2.8 cm^3 for ABH, 2.1 cm^3 for ABV, 1.8 cm^3 for FHB, and 3.1 cm^3 for FDB. Relative ratios could not be calculated as there were no events of increased muscle size greater than the calculated MDC in the CG, while the IG had an absolute risk of AR=0.39 for ABH, AR=0.31 for ABV, AR=0.15 for FHB, and AR=0.08 for FDB.

There were no significant differences in ACSA between the study groups after 8 weeks of intervention (ABH $p=0.100$; ABV $p=0.256$; FDB $p=0.169$; FHB $p=0.053$). At baseline, there were no differences between the groups for ACSA of any muscle studied (ABH $p=0.104$; ABV $p=0.142$; FDB $p=0.267$; FHB $p=0.066$). Calculated MDCs of 46.1 mm^2 for ABH, 31.9 mm^2 for ABV, 38.6 mm^2 for FHB, and 36.4 mm^2 for FDB showed no differences higher than the MDC between T8 and T0 in the CG, then the relative ratios could not be calculated. In the IG, no differences greater than the MDC was found for ABH, while absolute risk of the ABH was AR=0.08, for FDB AR=0.08, and for FHB AR=0.23.

Table 3- Mean, standard deviation, Cohen d effect sizes, p-values for repeated measure ANOVAs of ACSAs, and muscle volume. Intervention group (IG) and control group (CG). Abductor digiti minimi (ADV), flexor hallucis brevis (FHB), abductor hallucis (ABH), flexor digitorum brevis (FDB).

	Group	Muscle Volume (cm³) T0	T8	p-value	Cohen's d	Muscle ACSA (mm²) T0	T8	p-value
ABH	CG	15.4±8.1	13.3 ± 6.3	0.019	0.655	157.7 ± 79.8	145.2±64.6	0.100
	IG	11.0±6.1	13.7 ± 6.3			135.8 ± 64.4	141.2±58.5	
ABV	CG	12.5±4.6	12.0 ± 4.6	0.013	0.512	119.3 ± 33.7	113.9±31.7	0.256
	IG	9.2±5.0	11.2 ± 4.8			105.4 ± 36.1	112.8±31.4	
FDB	CG	14.0±4.6	13.3 ± 4.3	0.039	0.638	128.3 ± 44.4	122.0±44.1	0.169
	IG	10.4±4.6	12.5 ± 4.7			116.9 ± 45.5	116.7±30.8	
FHB	CG	12.6±3.6	12.0 ± 4.1	0.009	0.387	174.9 ± 37.6	166.2±52.2	0.053
	IG	9.1±4.8	10.2 ± 4.4			143.3 ± 38.9	147.2±42.3	

Propulsive impulses

There was a significant group-time interaction effect for vertical impulse in favor of the IG (p = 0.021). The post-hoc test revealed a significant difference (p = 0.007) between groups at baseline (Table 4). The MDC calculated for vertical impulse was 2.02 BWxs, without any participant showing differences higher than the MDC in the CG and an absolute risk of AR=0.08 for the IG. There was no significant difference between groups for antero-posterior impulse over time (p = 0.315). MDC resulted in 2.05 BW.s with relative risk ratio of RR=0.93, and a non-significant confidence interval CI=[0.15-5.63].

Table 4- Mean, standard deviation, Cohen d effect sizes, and p-value for propulsive vertical and antero-posterior impulses in BW multiplied by seconds.

Impulse	Group	T0	T8	p-value	Cohen's d
Vertical Impulse (BW x s)	CG	74.27±6.99	73.49±6.47	0.021	0.367
	IG	65.86±7.91	67.85±9.89		
Anteroposterior Impulse (BW x s)	CG	6.17±1.26	6.14±1.73	0.315	0.365
	IG	5.89±1.29	6.33±1.75		

MLA range of motion

There were no significant differences between groups for MLA range of motion after 8 weeks of intervention (CG T0=4.6°±2.2°; T8= 4.6°±1.8°; IG T0=4.2°±2.4°, T8=3.6°±2.3°; p=0.338). There was no significant difference between the groups at baseline (p=0.459). Calculated MDC of 3.43° resulted in a relative ratio RR=0.46, meaning 54% reduction in relative risk for events in the CG with a non-significant confidence interval CI = [0.12-11.35].

MLA Stiffness

No significant differences were found between groups for MLA stiffness (kmid) after 8 weeks of intervention (p=0.781) (Figure 3). Calculated MDC of 57.8 N/cm.kg2/3 revealed absolute risk of AR=0.23 for the IG and relative ratios could not be calculated as there were no events of increased stiffness higher than the MDC in the CG.

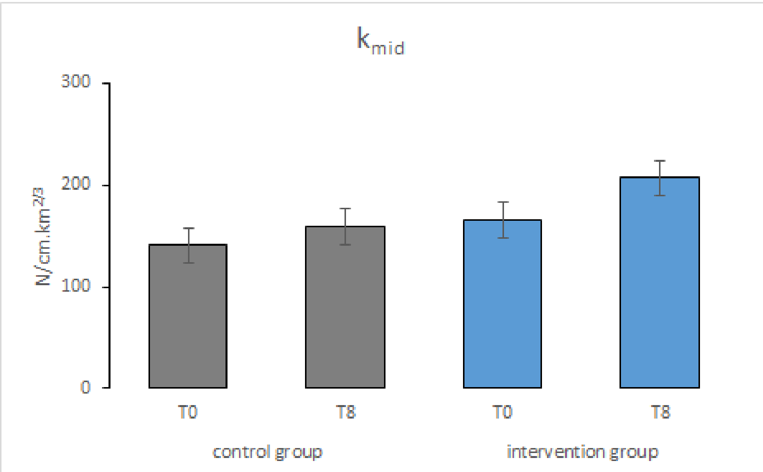

Figure 3- Arch stiffness (kmid) scaled by body mass (N/cm.kg2/3 according to Holowka, Wallace, and Lieberman(Holowka, Wallace, & Lieberman, 2018).

Correlations

Pearson's correlation analysis was used to assess the relationships between variables of foot strength, muscle volume, kmid, MLA range of motion, and vertical and antero-posterior impulses at baseline (T0) for all groups together (figure 4). Significant correlations were found for vertical impulse and muscle volume of the ABH (r^2=0.160; p=0.038), ABV (r^2=0.170; p=0.033), and FDB (r^2=0.480; p<0.001), indicating that the stronger the intrinsic foot muscles, the more vertical impulse a participant can produce during running. There was also a significant correlation between vertical and antero-posterior impulses (r^2=0.183; p=0.026). Each intrinsic foot muscle volume studied showed a significant direct correlation with the others, as shown in Figure 4.

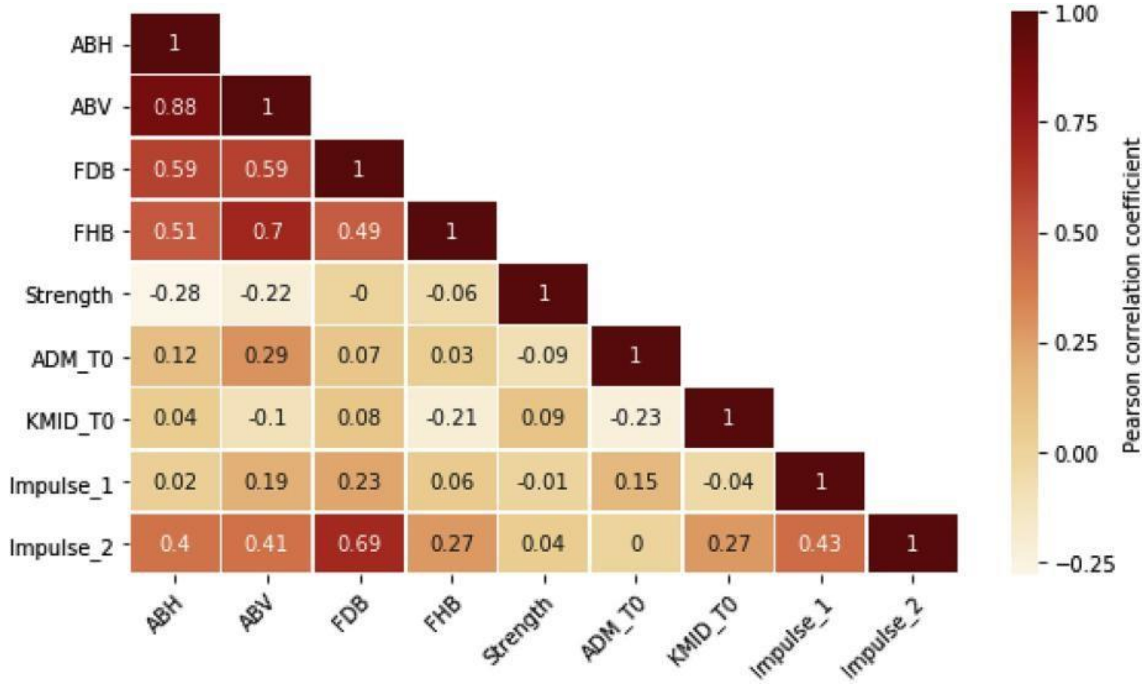

Figure 4- Heatmap of the Pearson's product moment at T0 for all groups together between MLA stiffness (KMID), vertical (IMPULSE1) and horizontal (IMPULSE2) impulses during stance phase, MLA range of motion (MLA_ROM), flexion strength of the hallux and toes (Strength), and muscle volume of the intrinsic foot muscles (ABH, ABV, FDB, and FHB).

Pearson's correlation tests were performed for the IG using the differences (delta) between T8 and T0 to verify relationships with muscle morphology changes (figure 5). Significant positive correlations between ABV muscle volume and antero-posterior impulse (r^2=0.370, p=0.031) was observed and an inverse relation between arch stiffness and arch range of motion (r^2=0.452, p=0.020) was observed.

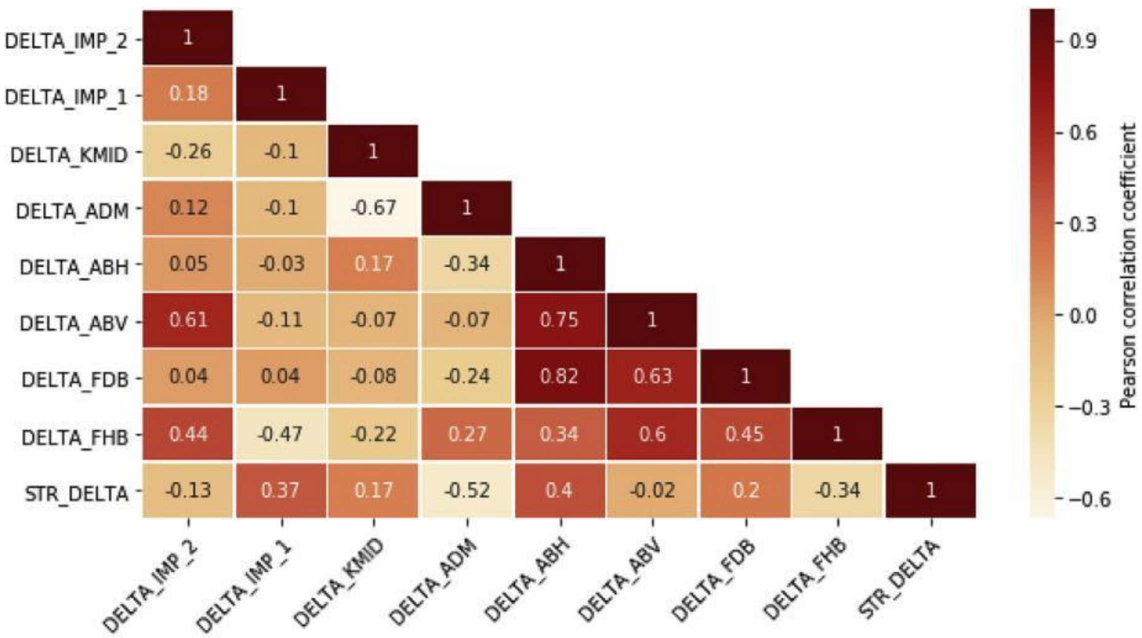

Figure 5- Heatmap of Pearson's product moment using the differences between T8 and T0 only for the IG between the variables of MLA stiffness (DELTA_KMID), MLA range of motion (DELTA_ADM), vertical (DELTA_IMP_1) and horizontal (DELTA_IMP_2) impulses during stance phase, flexion strength of the hallux and toes (STR_DELTA), and muscle volume of the intrinsic foot muscles (ABH, ABV, FDB, and FHB).

Regarding the adherence to the intervention, from a potential complete adherence (100%, i.e., 112 sessions), we accounted for 90 completed sessions corresponding to 80.4% adherence to the intervention. The average number of sessions attended in 8 weeks was 6.9±1.6.

Discussion

In this proof-of-concept randomized controlled trial, we investigated the effects of a foot strength training program on muscle morphology and strength as well as foot biomechanics in recreational long-distance runners. Our hypothesis that 8 weeks of training would increase intrinsic foot muscle volume and ASCA was confirmed for the volume of all studied muscles but not for ACSA.

Regarding the role of the intrinsic foot muscles during running, it was shown that if the plantar muscles are not properly activated during walking and running, the distal foot joints will not be stiff enough to transmit propulsion forces for push-off during late stance(Farris, Kelly, Cresswell, & Lichtwark, 2019). This led us to hypothesize that any noticeable changes in running mechanics after intrinsic foot muscle training would appear during late stance. The significant increase in the propulsive VGRF impulse while running confirmed this hypothesis, but not the AP-GRF impulse for the IG after 8 weeks. These main results show that 8 weeks of specific foot strength training targeting the intrinsic foot muscles can improve intrinsic muscle volume and running mechanics in recreational runners.

We found no significant effect of the training program on hallux and toe muscle strength using the pressure platform measurement, despite a significant increase in the volume of all intrinsic foot muscles. This finding might be due to the nature of the strength test, which demands specific motor control and activity of the extrinsic muscles, neither of which were included in the foot exercise protocol.

While ACSA increased in the IG group over 8 weeks, this change was not significantly different compared to the CG. This result is possibly explained by the irregular shape of the intrinsic foot muscles interfering with the way ACSA is calculated. Being the average of all slices containing the intrinsic foot muscles of interest throughout the foot scan, an increase in just one section of the muscle is attenuated by the other sections, which could make the gains statistically non-significant. Indeed, MDCs for the muscles' ACSA were higher than MDCs found for muscles' volumes. In a study by Chang et al.(Chang, Kent-Braun, & Hamill, 2012), atrophy of the intrinsic foot muscles attributed to the presence of chronic plantar fasciitis affected only the forefoot muscles with a 5.2% decrease in volume and an effect size of 0.26, while no differences were observed in rearfoot and total foot ACSA. Another explanation could be that with hypertrophy, muscle tissue can be measured in slices where previously they could not be. This also increases the number of slices containing the muscles measured, mitigating the results when calculating the average, even though a noticeable increase has occurred.

Increases in muscle volume and vertical impulse in the IG indicated that training the foot muscles can indeed alter running performance. Pearson's correlations using the difference between T8 and T0 for the IG revealed a correlation between ABV volume increase and antero-posterior impulse, although there was no significant interaction in the repeated measures ANOVA. Increased impulse could be beneficial for running performance, as found by Hunte, Marchall, and McNair,(Hunter, Marshall, & McNair, 2005) who assessed 36 athletes performing maximum-effort sprints and concluded that increased vertical impulse resulted in increased sprint velocity. Similarly, Munro, Miller, and Fuglevand(Munro, Miller, & Fuglevand, 1987) found that all VGRF descriptor variables increased significantly with running speed.

Similar results were found by Unger and Wooden (Unger & Wooden, 2000) after training the foot and investigating the effects on vertical and horizontal jumping performance. The authors found a significant increase in jump performance after 6 weeks of a toe flexor strengthening program in healthy physically active subjects, who also trained using similar exercises to those included in our protocol. Goldmann et al. (Goldmann, Sanno, Willwacher, Heinrich, & Brüggemann, 2012) also found an enhancement in jump performance after 7 weeks of toe flexor muscle training in healthy males.

We did not observe changes in MLA stiffness or mechanics after the intervention nor any significant correlation between MLA stiffness and the studied variables, even though increased values for stiffness greater than the MDC were seen in the IG only. Combining kinematic and kinetic measurements during gait in the MLA stiffness calculation, Holowka, Wallace, and Lieberman (Holowka et al., 2018) showed that different populations (minimally-shod men from northwestern Mexico and conventionally-shod urban American men) had different MLA stiffnesses. Although they were able to see differences in stiffness between samples, the MLA stiffness measured was probably the effect of different lifelong habits and factors of the two very different populations. It is not certain that the same variable will be sensitive to short-period interventions such as the one in our study, which led to changes in morphology of the foot muscles but did not have the same effect size as years of barefoot activities in rough terrain, as found by Holowka et al. (Holowka et al., 2018). Therefore, further studies could focus on other variables that are possibly more responsive to foot training and intrinsic foot muscle activation during running.

Regarding the FHSQ, the lack of significant differences between groups throughout time might have also another meaning that is the inaccuracy of the chosen instrument for the studied population. As an example, for almost all the subjects assessed the Foot Function domain showed the top score at T0 and T8. If the studied population had been different regarding foot function/dysfunction or even less physically active, perhaps these results would differ, as instead of increasing performance, they would restore their foot functionality.

The attendance to the locally supervised training in the IG was considered high and satisfactory, as the runners in the IG presented 80.4% as adherence. This rate was almost above 80%, which is a threshold to consider a successful adherence ("Oxford Centre for Evidence-based Medicine - Levels of Evidence (March 2009) - CEBM," n.d.).

Certain limitations exist for this study. Subjects had not previously tested for hallux and toe flexion strength using the method employed, and thus they had to learn how to avoid leaning their trunk forward or sideways or clawing their toes. After having their stance corrected by the assessor, they were successfully able to avoid these two mistakes. However, when participants pressed their toes and hallux against the pressure platform as hard as they could, they tended to also raise their foot arches and naturally shift their BW towards the calcaneus. Without leaning the trunk, a stronger participant could reach a maximum force value without losing their balance, although they had the capacity to press harder. To prevent this sort of bias, it would be wise to use a method closer to the one described by Ridge et al., (Ridge, Myrer, Olsen, Jurgensmeier, & Johnson, 2017) which used a dynamometer to assess arch doming and hallux and toe pulling strength with an apparatus that constrains the foot.

Another limitation arose from the differences in FDB muscle volume at baseline between the two groups (p=0.028). This measurement was significantly smaller for the IG, which might have affected the foot strengthening results, as weaker muscles may be more responsive to training than stronger muscles. None of the other muscles showed significant group differences at baseline.

Despite these limitations, this proof-of-concept study clearly showed that the foot training protocol effectively increased intrinsic foot muscle morphology, which may have led to the changes in propulsive impulses found in the IG, since these act as a stiffer spring during late stance(Luke A Kelly et al., 2018; Riddick, Farris, & Kelly, 2019). This mechanism is reinforced by the significant correlations found between muscle volume and vertical impulse, which may result in better performance and less energy expense during running.

Conclusion

The 8-week foot exercise protocol effectively increased intrinsic foot muscle volume and improved vertical running propulsive forces in recreational long-distance runners. This shows that intrinsic muscle strengthening affects running mechanics and suggests that it may improve running performance.

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6. MANUSCRIPT 3 SUBMITTED FOR PUBLICATION

Foot-core training for preventing running-related injuries: a survival analysis of a single-blind randomized controlled trial

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ABSTRACT

Objectives: Running-related injuries (RRIs) are a pervasive menace that can interrupt or end the participation of recreational runners in this healthy physical activity. To date, no satisfactory treatment has been developed to prevent RRIs. Here, we report the results of a new protocol, based on a ground-up approach focused on strengthening the core muscles of the foot, for RRI treatment and prevention.

Methods: A 12-month randomized single-blind parallel controlled trial was designed to investigate the effects of a foot-training protocol on the incidence of RRI in recreational long-distance runners. The participants, 118 runners, were assessed at baseline and randomly allocated to either an intervention (n=56) or control (n=62) group. The intervention group received an 8-week course of training focused on the foot-ankle muscles. The training protocol included 12 exercises performed 3 times a week. Assessments consisted of three separate biomechanical evaluations of foot strength and foot posture, and a weekly report on each participant’s running distance, pace, and injury incidence over 12 months.

Results: Subjects in the control group were 2.42 times (95%CI 1.98-3.62) more likely to experience an RRI within the 12-month study period than subjects in the intervention group (p=0.035). In addition, *time-to-injury* was significantly correlated with Foot Posture Index (p=0.031, r=0.41) and *foot strength gain* (p=0.044, r=0.45) scores.

Conclusion: Strengthening the foot core successfully prevented overall RRI in recreational runners**.** To better understand the biomechanical mechanisms, types of injuries for which this training is effective, and subgroups of runners, which might benefit the most, further study is recommended.

Keywords: Running, Sports injuries, Exercise therapy, Foot, Strengthening, Biomechanics

1. INTRODUCTION

Recreational running can be considered a “hero”[1–3] in the quest for better quality of life. As a means to achieve the well-documented health and anti-aging benefits of exercise [1,4], running is affordable, easy to learn and practice, and among the most popular physical activities worldwide.[5–7] However, as recreational running grows in popularity, it does so in a "hero-villain" manner, with its own vicious nemesis that grows as proportionally: running-related injuries (RRIs). Running carries the risk of several types of RRI, possibly leading to chronic impairment[8–10]. Annual RRI incidence for long-distance runners can be as high as 79.3%[9] and can lead to interruption or discontinuation of the practice. Many typical actions taken by runners to prevent RRIs[11], such as warm-up, cool-down, and stretching exercises, lack scientific evidence of effectiveness[12–14].

Although many studies have investigated different conditions and behaviors searching for RRI's risk factors, a review by Hulme et al.[15] investigating risk ratio on modifiable and non-modifiable possible risk factors reported that among many studied risk factors (frequency, pace and interval, body weight and body mass index, dietary plan and hormonal status, use of orthotics, stretching, warming up, cooling down, surface, etc) only a previous RRI and irregular or absent menstruation were associated with an increased risk of RRI.

Studies on interventions to reduce RRIs have yielded lackluster results. For instance, a graded training program, with a slow increase in running mileage based on the hypothesis that rapid mileage increase is an important RRI risk factor, found no differences between the intervention and control groups [16]. Interventions based on online advising found to be ineffective by Fokkema et al.[17] when addressing each participant's RRI risk factors, including personal, training, biomechanical, and equipment factors. However, Hespanhol Jr et al.[18] were able to see a 13% reduction in RRIs in a group receiving specific advice built upon their RRI status throughout 6 months of follow up. But, the effects of this intervention on preventive behaviors investigated (warming up, choosing specific footwear, implementing general conditioning training, etc) were considered non-significant. A better outcome was obtained in a controlled trial[19] that investigated whether wearing motion-control running shoes could minimize injury risk in recreational runners with supinated, neutral, and pronated feet; however, RRI risk was decreased only in participants with pronated feet that received motion control running shoes compared to the control group on standard shoes (hazards ratio=0.34; 95% CI 0.13 to 0.84). The authors concluded that, with cushioned shoes, better motion control might be needed to limit injury risk. However, this begs the question: isn’t foot-ankle motion control exerted by runners themselves? Even if cushioned shoes restrain the runner’s capacity for movement control or demand more of the foot-ankle muscles, shouldn't it be possible to address this directly, through training?

In fact, training and strengthening of foot-ankle muscles, with the aim of improving postural control and balance, have already proven to be effective in other patient populations. In a study addressing the link between falls and foot deformities or intrinsic foot-muscle weakness in the elderly, foot-core[20] training was shown to benefit older people at risk of falling with a factor of 7[21]. In a study seeking to improve athletic performance, the jump performance of young athletes significantly improved after isometric training of the hallux flexion for seven weeks[22]. Both of these studies demonstrate the benefits of strengthening the foot core muscles for general body function and balance. Because foot muscles play an intrinsic role in dampening impact and propelling the body forward during running[23–25], it is reasonable that training could improve these functions, and that this could serve to prevent RRIs. Therefore, the aim of this randomized single-blind controlled trial was to investigate the efficacy of a novel foot-muscle strengthening protocol in reducing the incidence of RRI in recreational runners over the course of a one-year follow-up.

2. METHODS

A 12-month randomized single-blind parallel controlled trial was designed to investigate the possible benefits of a foot-muscle training protocol in reducing RRI incidence in recreational long-distance runners (figure 1). A detailed description of this protocol, following CONSORT recommendations, has been published elsewhere [26]. The definition used for RRIs was that of Macera et al.[27]: any musculoskeletal pain or injury caused by running practice that induces changes in the form, duration, intensity, or frequency of training for at least one week.

2.1 Participants and recruitment

Sample-size calculation was conducted using a chi-squared statistical design for the primary outcome (between-group differences in RRI incidence) based on a previously recorded annual lower-limb RRI incidence of 28%(8), statistical power of 80%, and level for significance of p=0.05.[28] This yielded a requirement for 101 subjects. Assuming a 10% total dropout rate, we aimed to recruit at least 112 subjects. Subjects were recruited between August 2015 and August 2017 through digital social media advertising and direct contact with runners and running groups in the university surroundings. Eligibility criteria included runners between 18 and 55 years old, who had been running for at least one year, at least 20 km per week, and no more than 100 km per week, with no RRI in the 2 months prior to baseline assessment, no experience running barefoot or in minimalist shoes, and without chronic diseases or impairments that could influence running performance, such as osteoarthritis.

Participants signed an informed consent form approved by the Ethics Committee of the School of Medicine of the University of São Paulo (number 031/15). Participants were randomly allocated to Intervention or control groups after baseline assessment. Using Clinstat software (University of York, Heslington, UK)[29], random blocks up to 8 in size were created, dividing 120 potential participants into IG or CG. The codes for the groups were kept in opaque and sealed envelopes numbered 1 to 120, and the researchers involved in the allocation and assessments were blind to the group codes and block size. After the runners' agreement to participate and be assigned in the research, an independent researcher also blind to the codes performed the allocation into the groups. Allocation was performed in order of assessment, which were scheduled over two weeks expecting no-shows. The last 2-weeks of assessment summed a total of 118 allocated subjects, surpassing the 112 previously calculated.

2.2 Participants and public involvement

Runners were not involved in the research process.

2.3 Treatment arms and assessments

Participants allocated to the intervention group received eight weeks of training focused on the foot-ankle muscles, with 12 exercises progressing weekly in volume and difficulty[26]. Participants were trained once a week by a physiotherapist and given online access to the exercises' descriptions and videos to perform the same exercises an additional 3 times per week, remotely supervised by the same physiotherapist. Participants allocated to the control group were instructed to perform a 5-minute placebo static stretching protocol 3 times per week based on online descriptions and images[26]. Both groups were instructed to perform their respective exercises 3x/week up to the end of the 12-months follow up and register their adherence in the web-software. (After the results indicated effectiveness, the foot training was offered to all participants at the end of the study.)

Assessment consisted of three evaluations: at baseline, 8 weeks, and 16 weeks, and a weekly report on participants' running distance, pace, and RRI for 12 months (incidence and *time-to-injury* were reported) (figure 1). Before baseline assessment, each participant ran barefoot at self-selected speed on a treadmill while being filmed at 200 Hz by a camera placed laterally. The Foot Posture Index (FPI)[29] was measured at baseline. During each evaluation, foot strength was measured by pressing the hallux and toes against an emed pressure platform (novel, Munich, Germany), as described previously[30]. *Foot strength gain* was defined as flexion strength at the 8-week evaluation minus flexion strength at baseline. Participants received an explanation on the definition of RRI and in the event of a reported injury, the physiotherapist scheduled an assessment to determine if the reported injury fitted the definition by Macera et al.[27]. Participants were also contacted if their monthly reported running mileage was too low or missing. Adherence to the supervised intervention was assessed weekly in the first 2 months, and then monthly thereafter, using web-based software developed for this project. Adherence to the remotely supervised training (3 times a week) was monitored using the same web-software and reinforced of its importance at every contact with the subjects.

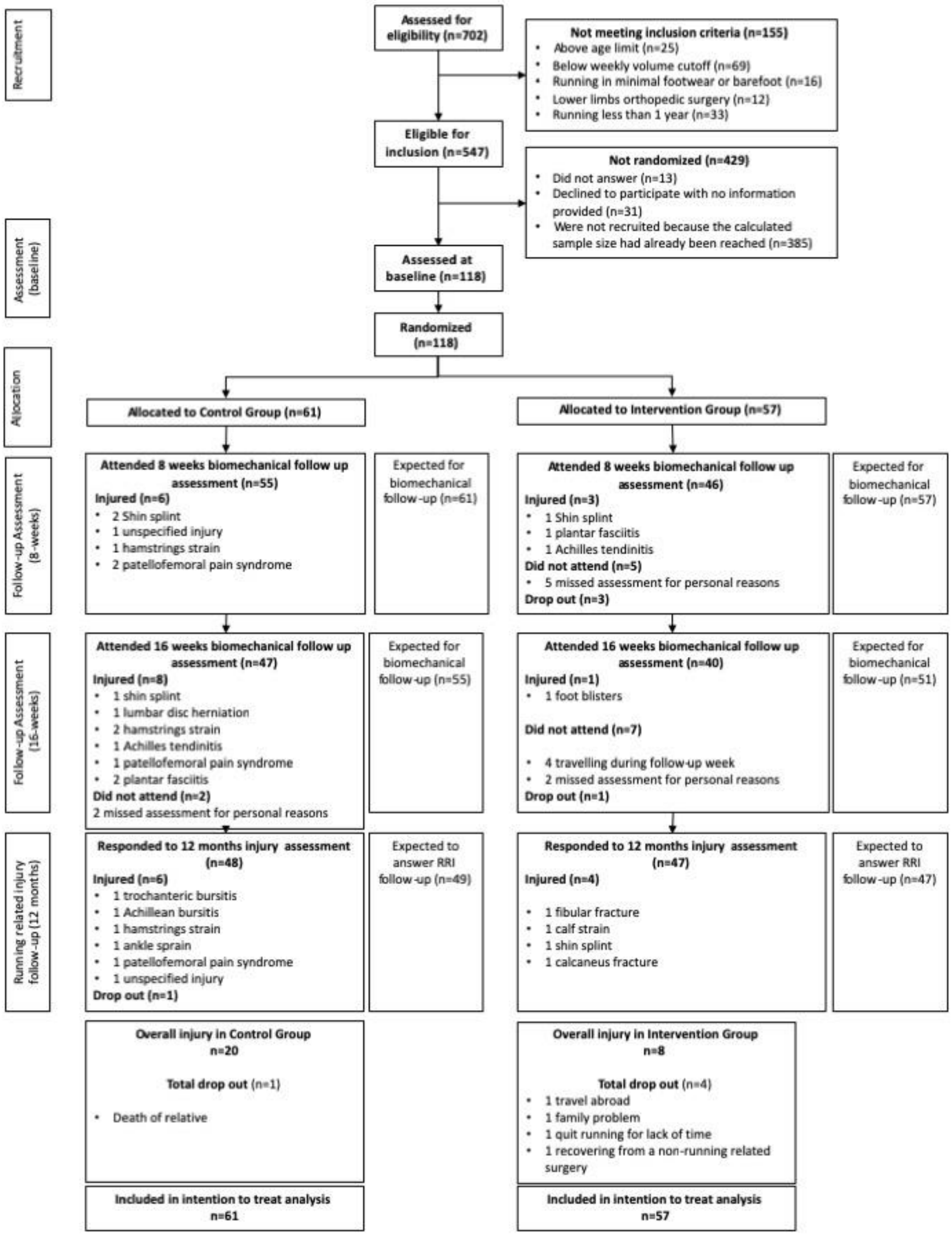

Figure 1. Flow chart of recruitment, assessment and follow-up process.

2.4 Statistical analysis

An intention-to-treat analysis was performed and the following procedures were applied for this aim.

To identify any post-allocation between-group differences, descriptive statistics and t-tests were performed (with Pearson's correlation coefficient calculation) for controlling independent variables (age, BMI, Arch Index, and FPI), and Chi-square tests were used to compare dichotomous variables, at baseline. Any significant correlation larger than 0.30 between a controlling variable and the *time-to-injury* variable(32) was included in the survival analysis. Kaplan-Meier survival analysis was used to identify differences in RRI risk between allocation groups (intervention vs. control) at 12 months. An event was defined as any RRI recorded within the 12-month follow-up. Data for participants lost to follow-up for any reason were recorded as censored data from that time on (e.g., dropouts). Log-rank tests were performed for comparing RRI risk between groups at 12 months and at each bimester. Cox proportional hazards ratio was calculated to estimate RRI risk at 12 months. To account for RRI risk factors described in the literature[9,15,33], Cox proportional hazards models were used to impute covariates: (i) previous RRI, (ii) BMI, and (iii) running volume. Due to non-normal distribution of the variable, mean *time-to-injury* for the follow-up period was compared between groups using the Mann-Whitney test. Quartile estimation was used to calculate the survival time at which a chosen percentage of the population was injured, a feature of interest derived from comparison of mean *time-to-injury* for the two groups. Thus, we calculated the survival time at which 25%, 50%, and 75% of the population got injured. Then, Mann-Whitney tests were used for between-group comparisons.

Additional Kaplan-Meier plots were performed to verify the influence of previous RRIs on one-year survival probability, using RRIs as a stratification variable (0=absent, 1=present) for the subjects allocated to the control group. This analysis was performed to avoid factors confounding intervention results with RRI history, since a previous RRI is the strongest risk factor for injury[9,15,33,34]. In addition, the Kaplan-Meier method was applied to verify the influence on RRI risk of any variable that showed correlation with *time-to-injury*.

3 RESULTS

3.1 Baseline characteristics and correlations

Of the 118 runners assessed at baseline (61 males, 57 females), 57 were allocated to the intervention group and 61 to the control. There were no differences between groups in any of the controlling independent variables at baseline (Table 1). On average, running volume was similar for runners in the two groups throughout the study period (60-110 km per month) (Figure 4 in the supplementary material). A median follow-up time of 12 months and interquartile range of 3 months. To assess whether variability in running volume across runners had an effect on the survival analysis, we performed a Kaplan-Meier analysis with a log-rank test using reported mileage instead of follow-up time, which showed that there were no differences in RRI risk between groups over 500 km ran (p=0.088) neither over 1000 km ran (p=0.110).

Table 1. Mean and standard deviation for both groups of controlling variables: anthropometric, demographic and training outcomes in baseline. M: male; F: female. L: left; R: right. Effect sizes were calculated using Cohen's d for continuous variables* and r^2 for discrete variables†.

Characteristics	Unit/qualifier	Control group (n=61)	Intervention Group (n=57)	Effect size (CI 95%)
Participants' characteristics				
Age	Years	41.3 ±6.85	40.5 ±7.9	0.11 (-0.25 – 0.47)*
Height	cm	171.0 ±9.1	167.4 ±8.2	0.21 (0.05 – 0.78)*
Body mass	kg	72.1 ±13.2	68.2 ±12.3	0.30(-0.07 – 0.69)*
Sex	Male Female	33 29	28 28	0.03 (-0.15 – 0.21)†
BMI	kg/m²	24.5±3.2	24.2±2.9	0.10 (-0.28 – 0.48)*
Running experience	Years	6.9±5.8	5.4±4.7	0.28 (-0.09 – 0.67)*
Foot Posture Index	Arbitrary units Median, min: max	R= 2,-6:9 L= 2,-6:9,	R= 0,-7:10 L= 1,-7:10	0.16 (-0.03 – 0.34)† 0.19 (0.01 – 0.36)†
Arch Index	Arbitrary units	R= 0.20±0.06 L=0.18±0.087	R= 0.18±0.07 L= 0.16±0.07	0.09 (-0.01 – 0.47)* 0.06 (-0.02 – 0.39)*
Foot strike pattern	% Rearfoot % Non-rearfoot	78.7 21.3	75.4 24.6	0.04 (-0.02 – 0.05)†
Previous injury	% of total participants	32.7	45.6	0.13 (-0.05 – 0.30)†
Study participation pattern				
Running Volume	km/month	97.7 ±61.4	82.3 ±59.5	0.07 (-0.13 – 0.63)*
Running Pace	min/km	6.6±1.4	6.7±1.9	0.06 (-0.44 – 0.32)*
Protocol sessions participation	% of total sessions	NA	88.0	NA

FPI was significantly correlated with *time-to-injury* (r=0.41; p=0.031) (Figure 2), suggesting that the higher a runner's FPI, the longer it will take to develop an RRI. However, a Mann-Whitney test did not show significant differences in baseline FPI between injured and non-injured participants (right p=0.849, left p=0.583). *Time-to-injury* was also correlated with *foot strength gain* (r=0.45; p=0.044). Two other significant correlations were FPI with BMI (r=0.21; p=0.023) and running volume with pace (r=-0.32; p=0.001). Regarding running footwear**,** there were no significant differences for the heel-to-toe drop distance, heel stack height, or shoe mass between groups (Table 1, supplementary material). Chi-square tests showed no significant association between stack height (stratified according to four quartiles; p=0.903) or heel-to-toe drop distance (stratified according to four quartiles; p=0.887) and RRI incidence in our sample (n=118).

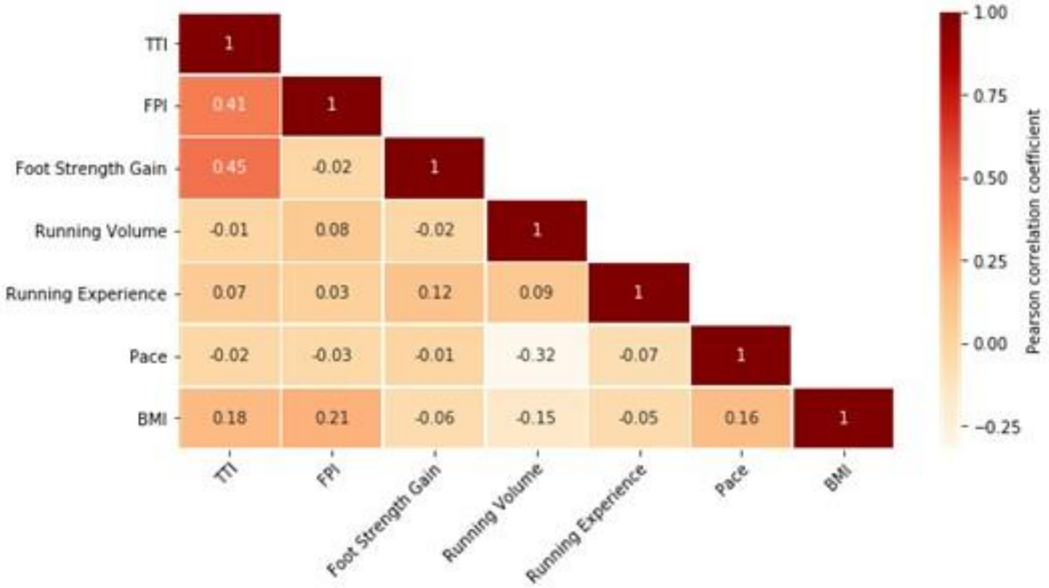

Figure 2. Pearson´s correlation coefficients of controlling variables. Foot strength gain was the difference between values measured in T0 and T8. Running Volume is the monthly average (km/month), Running Experience in years of practice, Time-to-injury (TTI) in m.

3.2 Running-Related Injury

RRI injury occurred in 28 participants (23.5%, 95%CI: 16.1-31.4%) within one year, 20 from the control group (16.9%, 95%CI: 10.2-23.7%) and 8 from the intervention group (6.7%, 95%CI: 2.2-11.3%). Details on the RRI characteristics are presented in Table 2.

Table *2*-Self-reported running-related injuries during the participation on the study.

	Control group (n=61)		Intervention group (n=57)	
	N	**Per cent**	**N**	**Per cent**
Injury location				
Foot-ankle	5	8.1	4	7.1
Legs	3	4.8	4	7.1
Knees	4	6.5	0	0
Thighs	4	6.5	0	0
Hips	1	1.6	0	0
Lower Back	1	1.6	0	0
Unspecified	2	3.2	0	0
Injury type				
Plantar fasciitis	2	3.2	1	1.8
Achillean bursitis	1	1.6	0	0
Achilles tendinitis	1	1.6	1	1.8
Ankle sprain	1	1.6	0	0
Calcaneal fracture	0	0	1	1.8
Foot blood blister	0	0	1	1.8
Shin splints	3	4.8	2	3.6
Calf strain	0	0	1	1.8
Fibula fracture	0	0	1	1.8
Patellofemoral pain	4	6.4	0	0
Hamstring strain	4	6.4	0	0
Trochanteric bursitis	1	1.6	0	0
Lumbar disc herniation	1	1.6	0	0
Unspecified injury	2	3.2	0	0

3.3 Survival analysis

The Kaplan-Meier survival estimates showed a significant difference in the log-rank test between groups at 12 months (p=0.027) (Figure 3A). Log-rank analysis comparison by bimesters (Table 3) showed significant differences between groups after just 8 months of follow-up. A Cox proportional hazards analysis resulted in a hazard ratio of 2.42 (p=0.035, 95%CI 1.980-3.620), meaning that control subjects were 2.42 times more likely to experience an RRI than subjects in the intervention group after one year.

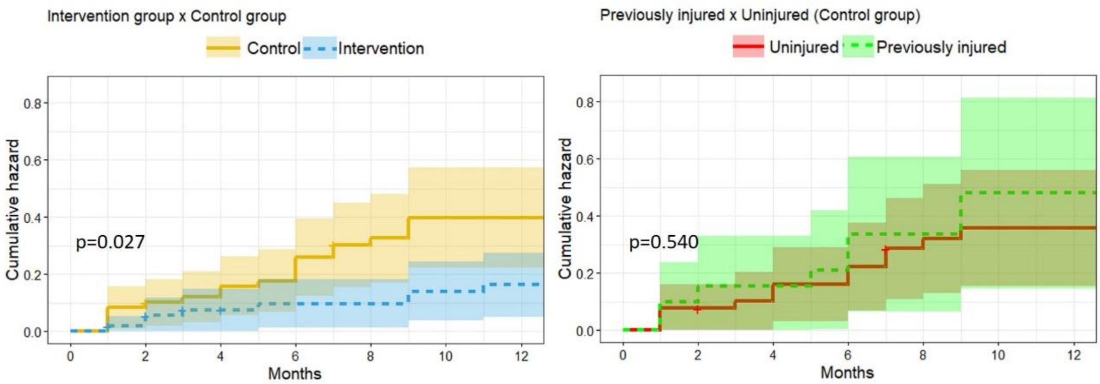

Figure 3. Kaplan-Meier survival plots. (A) The cumulative hazard in yellow for the control group and in blue for the intervention group. (B) Analysis between previously injured and uninjured participants for the control group only. Log-rank tests did not show significant differences between groups.

Table 3. Cumulative survival probability in each follow up bimester for the control group and the intervention group. Log-Rank tests show significant differences between groups after 8-months follow-up. Cumulative risk difference calculated as the injury risk in the CG minus in the IG.

Cumulative survival probability	**2 months**	**4 months**	**6 months**	**8 months**	**10 months**	**12 months**
Control group	0.9180	0.8846	0.8012	0.7511	0.6658	0.6658
Intervention group	0.9455	0.9269	0.9076	0.9076	0.8690	0.8497
Log-Rank (p)	0.3748	0.2113	0.0565	0.0153*	0.0150*	0.0273*
Cumulative risk difference	2.75%	4.23%	10.64%	15.65%	20.32%	18.39%

* Represents significantly p-values

The Cox proportional hazards regression was performed considering the risk factors as covariates. With age as a covariate, every increase in one year of age was associated with a 1.07-fold increase in RRI risk (p=0.015; 95%CI 1.013-1.129). Other covariates analyzed (previous injury, BMI, strike pattern, sex, FPI, years of practice, mileage, and pace) did not significantly affect RRI risk ($p>0.05$). A Kaplan-Meier analysis was performed to verify the influence of previous RRI history on one-year survival probability for the control subjects. Although described elsewhere as a risk factor for RRI[9], suffering a previous RRI did not significantly affect RRI risk in our sample (log-rank test $p=0.540$) (Figure 3B).

Because a significant correlation was found between FPI and *time-to-injury,* a Kaplan-Meier analysis was performed to verify the influence of FPI on one-year survival probability using FPI as stratification variable. (FPI values were classified from lower to higher and divided into two equal groups for this analysis: $-7 \leq x \leq 1$ and $1 < x \leq +10$). The log-rank test did not show significant differences between RRI risk and FPI ($p=0.942$).

The Mann-Whitney test comparing the average months until RRI occurrence showed no significant difference between groups ($p=0.758$). As for the quartile-estimation calculation of survival time at which a chosen percentage of the population was injured, since the total RRI percentage in the follow-up was 23.5%, a best quartile estimate would be 25%. The mean *time-to-injury* of 25% of the population was 7.63±2.60 months for the control group and 10.15±2.69 months for the intervention group.

3.4 Adherence

Regarding adherence to the supervised intervention, measured as the attendance to the locally supervised training, participants in the intervention group were expected to attend supervised training with the designated researcher once a week. Complete adherence to the supervised intervention would be all 57 subjects attending all 8 sessions; i.e., 456 completed sessions for 100% adherence. Subtracting subjects who were injured during the intervention, 100% adherence would be 432 completed sessions. Therefore, the recorded attendance of 380 completed sessions corresponds to 88% adherence to the supervised intervention. The average number of sessions attended in 8 weeks was 6.6±2.0.

Participants in the IG were instructed to perform 16 remote exercising sessions for the first 8 weeks (2 sessions weekly, in addition to the supervised session), then we expected them to perform 24 remote sessions every eight weeks to the end of the study (3 sessions weekly) after the first 8 weeks of intervention. To calculate adherence to the remotely supervised training, we averaged the sessions performed every eight weeks by 16 between T0 and T8, and by 24 after the first 8 weeks, and report the adherence rate in percentage. The adherence to the remote intervention sessions was on average 90.4% in the first eight weeks (T0 to T8), 83.5% between T8 and T16, 68.5% between T16 and T24, 62.5% between T24 and T32, and 48.9% between T32 and T40.

4. DISCUSSION

4.1. Preventing RRI by strengthening foot core muscles

Our hypothesis that a foot-core exercise protocol could reduce the incidence of RRIs was confirmed: the control group suffered significantly more RRIs than the intervention group, with a risk of 2.42-fold higher. The only relevant independent controlling risk factor found to be significantly predictive was age. Each year of increased age was associated with a 1.07-fold increase in RRI risk, in keeping with findings from previous studies[5,9,35].

By the fourth month of follow-up, both the control and intervention groups had started to differ in cumulative RRI risk, although statistical significance for survival probabilities was only reached in the eighth month. This pattern implies that 4–8 months of this specific foot exercise regimen might already be effective in reducing the risk of an RRI in recreational runners.

A gradual increase in load tolerance through repeated training with properly dosed gain in running experience has been shown to reduce RRI risk[36]. For example, a 4-week running program for obese novice runners that started with 3 km/week, compared with 6 km/week, reduced cumulative RRI risk by 16.3%[37]. The protection against cumulative RRI risk conferred by foot exercises in our study is not expected to appear immediately, because the increased load tolerance in the intervention-group runners stems from chronic muscle gain obtained through months of foot exercise.

4.2 Risk factors for RRI

Even though some RRI risk factors were controlled/excluded, we also included some previously described recurrent factors in the Cox proportional hazards models[38]: previous RRI[9,15,33], BMI[39–42], running experience,[15,33,37,39] and running volume[15,33]. However, these factors were unlikely to be responsible for the difference in RRI incidence between groups, since the effects on hazard ratio were not nearly as high as the protective effect of the intervention. Further, we performed statistical analysis to evaluate these factors' effects on RRI incidence[43,44]. One likely reason for the absence of relationships between known risk factors and RRI might be the eligibility criteria we adopted[26], with exclusion criteria such as novice runner and >30 BMI. We chose this specific population of recreational long-distance runners to gain better external validity, as this best represents the majority of the running population[45].

A significant correlation was found between FPI and *time-to-injury*, suggesting a protective effect of everted/pronated feet, as found by Nielsen et al.[46]. However, survival analysis using FPI as stratification variable found no difference. A key correlation was seen between *time-to-injury* and *foot strength gain*: the stronger the foot, the longer it took the runner to develop an RRI. Similar correlations have been seen between FPI and *time-to-injury*. Despite findings pointing to previous RRI as a risk factor for new RRIs[15,40,47], merely using it as a logistic covariate did not reveal a significant influence in our survival analysis.

4.3 Probable mechanisms of action of the foot-exercise program

Previous interventions for RRI prevention have focused on potential risk factors, such as repetitive mechanical loads while running[12,16,48]. Our innovative ground-up intervention approach targeted foot musculoskeletal strength and dynamics towards the goal of dampening loads while running, increasing the efficiency of the body to attenuate mechanical loads directly related to RRI[48–53]. The main hypothetic mechanism by which strengthening the intrinsic foot muscles protects against RRI is that a stronger foot should better dissipate excessive and cumulative loads through foot structure and the medial longitudinal arch, changing the function of the foot from a dampener in the early stance to a spring in the late stance[23,54].

4.4 Strengths and Limitations

Strengths of the study include rigorous RCT methodology, inquiry about injury rates on a monthly basis rather than depending purely on injury incidence proportions, and a supervised training approach, which increased adherence to the protocol (88%) and reduced drop-out rates. In addition, this is the first study to evaluate RRI risk associated with a specific foot-training protocol focused on improving intrinsic foot-muscle strength for non-novice recreational long-distance runners. Certain limitations exist for this study. We have not discriminated different types of RRIs in our analysis. Different RRIs or injury sites are expected to stem from different mechanisms, and enhancing foot strength might be more effective in preventing some types of injuries than others. Although we expect that the gains in intrinsic foot-muscle strength were the most important factor for our observed reduction in RRI incidence, other aspects of the training, such as information exchange during group sessions, nocebo effects, or placebo effects might also be relevant factors.

5. CONCLUSION

Our proposed foot-core exercises protocol and the regimen adopted in the program (one supervised and three at-home sessions per week) were effective in decreasing RRIs in the studied population by a factor of 2.42. This foot-exercise program already showed evidence of effective RRI risk reduction in recreational runners at just 4-8 months of training. Although the mechanisms underlying the observed reduction in RRIs are uncertain, future studies with larger sample sizes would allow for better elucidation of causalities through the opportunity to stratify the survival analysis by injury type or site. Inclusion of different populations of runners, biomechanical factors, musculoskeletal factors, and a longer follow-up time might provide more insights on subgroups for which the intervention is more beneficial and specific risk factors influencing the survival analysis.

6 STATEMENTS

6.1 Contributorship

All authors made substantial contributions to all three of sections. All authors contributed to (1) the conception and design of the study, acquisition of data, and analysis and interpretation of data; (2) the drafting of the article and critical revision for important intellectual content; and (3) the final approval of the version to be submitted. In the study, these authors took primary responsibility for the following roles: ICNS was responsible for the study design, interpretation of the data, writing the report, submission of the manuscript, and management. ABM and UTT were responsible for the study design, data collection, analysis, interpretation, writing the report, and submission of the manuscript. MD was responsible for the study design, interpretation of the data, writing the report, and submission of the manuscript. All authors contributed to the initial draft, revised the manuscript, provided feedback, and approved the final manuscript.

6.2 Competing interests

The authors affirm that this study did not receive any funding/assistance from a commercial organization with the potential to lead to a conflict of interest.

6.3 Funding

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6.4 Data sharing

All personal data from potential or enrolled participants were maintained as confidential before, during, and after the trial by encoding each participant's name. All data access and storage are in keeping with National Health and Medical Research Council guidelines, as approved. All non-confidential files are available at figshare.com (https://doi.org/10.6084/m9.figshare.10003406.v2)(53) The main researcher reported all important protocol amendments to investigators, review boards, and trial registration. Supported data are available upon request.

6.5 Ethics approval and consent to participate

This trial was approved by the Ethics Committee of the School of Medicine of the University of São Paulo (18/03/2015, Protocol # 031/15), according to the Declaration of Helsinki Ethical Principles for Medical Research Involving Human Subjects. It was registered at ClinicalTrials.gov (a service of U.S. National Institutes of Health) Identifier NCT02306148 (November 28, 2014) under the name "*Effects of Foot Strengthening on the Prevalence of Injuries in Long Distance Runners*". The main researcher explained to each eligible participant every step of the assessment and follow-up, possible risks, and that no compensation or benefits were to be expected. When agreeing to participate, participants were asked for written informed consent, according to standard forms.

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8 SUPLEMENTARY MATERIAL

Running volume

Figure 4. Monthly running volume average for 12 months for the Control and Intervention groups in kilometers. Bars represent standard deviation at each month.

Running Shoes

Table 1. Means, standard deviations and p-values (t-tests) of comparisons between groups of the participants' running shoes' characteristics for heel-to-toe drop distance, heel stack height and shoe mass. Effect sizes were calculated as Cohen d.

	Control Group	Intervention Group	p-value (t-test)	Effect Size
Heel-to-toe drop (mm)	9.74±1.18	9.66±1.81	0.819	0.053
Heel stack height (mm)	27.99±4.77	29.75±4.77	0.164	0.369
Shoe mass (g)	288.80±41.38	284.00±44.27	0.684	0.112

7 GENERAL DISCUSSION

This study was part of a larger theme project called "Biomechanics and functional aspects of the musculoskeletal system in runners: chronical effects of therapeutic exercises and aging". More of its results can be found in Caravaggi et al.(Caravaggi *et al.*, 2019) and are yet to be published, concerning the effects of IFM training on running kinematics and kinetics.

7.1 Feasibility of the protocol and randomized trial

The exercises protocol and clinical trial were proven feasible regarding all the factors considered: recruitment rate; recruitment success; participants' satisfaction with training; adherence to the training protocol; and the effect of the intervention in improving foot muscle strength and foot biomechanics.

Recruitment rate and success were not a restriction to the study because the number of runners willing to participate and share their data is very high. Even with the described eligibility criteria narrowing the numbers down, the long follow-up and requirements for displacement around the city (for training and MRI assessment), and no runner denied participation after the protocol was explained to them.

Another concern was if the exercising protocol was too difficult, too long or too tedious to be performed for as long as it was set to be (3x/week for 12 months). Participants in the intervention group had a good adherence to locally supervised training with no subjects excluded due lack of participation. As for the remotely supervised training, we noticed a drop in adherence after T16. When inquiring the subjects, we noticed that reported satisfaction with the protocol was similar in both groups (Manuscript 1, Figure 6) and when questioned about what would make the participants be more adherent and consistent to the interventions, most of them said that more information about the expected outcomes and mechanisms for possible changes would do so. We worry, though, that sharing that information could be both misleading (since we could not conclude anything in the beginning of the study) and could enlarge the approach and treatment between groups.

As we stressed in the feasibility paper, the values of foot strength, muscle area and other collected variables reported had limited validity and statistical power to infer conclusions on the whole clinical trial. Even so, no differences were found in foot strength and foot functionality on the feasibility study, and the differences in muscle volume were found, which later, with more participants analyzed, this difference was not confirmed. Regarding the foot kinematic variables during running, they were fairly comparable to what was described in the study by Portinaro et al. (Portinaro *et al.*, 2014).

7.2 Proof of concept – effect of the foot core program in the foot strength, functionality and running mechanics

The increase in muscle volume after the intervention was sufficient to show that the developed training protocol had an important effect on the intrinsic foot muscles. Not only the two-way ANOVAs showed significant increase in muscle volume for the intervention group but also a Bayesian approach only showed hypertrophy above minimal detectable changes for subjects in the intervention group. Although we found an increase in cross-sectional area of the foot muscles in the Manuscript 1, with the larger sample size of Manuscript 2 allowing us to perform inferential statistical tests, these differences were not significant. As discussed on Manuscript 2, the asymmetrical aspect of the intrinsic foot muscles had an important effect on the minimal detectable change.

We expected, as the intrinsic foot muscle volume increased in the intervention group, that the foot strength would also increase significantly. However, as we reported on study 2, neither the specificity nor the reliability of the measurement using the pressure platform were satisfactory for detecting changes in a healthy population. Even the researcher that proposed the method for evaluating foot strength on elders recently participated on the development of a different method for intrinsic foot muscles strength measurement (Garofolini *et al.*, 2019), as did other groups such as Ridge et al.(Ridge *et al.*, 2017).

The significant increase found on vertical running impulses in the IG is also a strong indication that the factors influencing injury incidence are indeed biomechanical rather than behavioral confounders such as training modifications not reported by participants. It also demonstrates that the foot exercises did have an effect on running mechanics, reinforced by the correlation found between ABV's volume (between T8 and T0) and running impulses.

With respect to foot health and foot function, the lack of differences found for both groups was clearly due the healthy aspect of our participants and the nonspecificity of the Foot Health Status Questionnaire. When questioned if they noticed any effect of the intervention, participants in the intervention group usually reported how old uncomfortable footwear they own were no longer painful, blisters would not form even after long races and calluses started disappearing.

Contrary what was expected, the dynamic strain of the foot's longitudinal arch during running calculated did not show differences after the intervention. It is possible that a longer period of training or even change of costumes like walking barefoot and running in rougher terrain, as did the population described by Holowka, Wallace and Lieberman (Holowka, Wallace and Lieberman, 2018), would change the dynamics of the foot arch.

One of the reasons by which such a simple calculation (kmid) for measuring arch stiffness was used by Holowka, Wallace and Lieberman (Holowka, Wallace and Lieberman, 2018) was an equipment limitation because they used a conventional video camera to record foot kinematics and a pressure platform to measure ground reaction forces. Because of that, the authors have to cope with some approximations such as presuming that at 50% of the stance phase would imply the ground reaction force to have only vertical components. It is possible that using a more reliable technic without such approximations would result in different findings. A more reliable method would be a *quasi-stiffness* technique described as the slope of the joints' moment-angle relationship, as used in Kern *et al*. (Kern *et al.*, 2019) and investigated by other researchers (Kelly, Cresswell and Farris, 2018; Farris *et al.*, 2019; Riddick, Farris and Kelly, 2019).

7.3 Effect of the Foot core training on RRIs incidence

For the duration of the study, participants were to report weekly their running volume, which was fairly accurate since the great majority of them used running apps and GPS watches to record mileage and speed and agreed to share the information for the duration of the research. For the intervention group, the only way participants had to report was using the developed web-software SAEC, which runners had to be frequently reminded to fill, even though automatic e-mails were sent whenever the participants were not to log in the week before. The drop on exercising sessions noticed after the 16th week of follow up (83.5% to 68.5% adherence) might have had an important effect on the outcomes of this study. The average running volume for both groups was kept fairly constant throughout the 12 months of follow up (Manuscript 3; Figure 4).

Supervised foot exercising sessions performed were also considered satisfactory overall. At the end of the study, the average number of sessions attended of the 57 participants in the intervention group was 6.6±2.0 (Figure 1) with the maximum being 8 sessions.

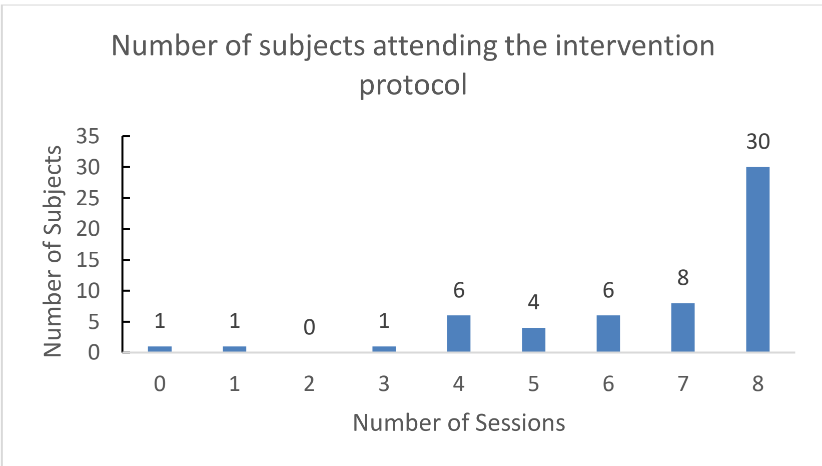


Figure 1. Number of supervised foot exercising sessions accomplished by participants in the intervention group. 30 participants were presented in all supervised sessions.

Three participants suffered a running related injury during the first 8 weeks of intervention (3, 5 and 7 sessions completed before injury) and three subjects dropped out also on the first 8 weeks of intervention (0, 1 and 4 session completed). The reasons given by the three subjects who dropped out during the intervention period was that (i) would not practice running anymore for lack of time, (ii) would travel to another country and miss the intervention and biomechanical assessments, and (iii) had personal reasons to interrupt the participation.

Adherence to the assessment at the end of the study was satisfactory and away higher than 85%. Subjects were contacted for rescheduling after not attending an assessment session and when asked for the reason of not attending which most often was related to the difficulty of living in a metropolis such as traffic congestion.

The main outcome of the study was quite surprising in its effect size, with a hazard ratio of 2.4, indicating that the CG had 2.4 times higher risk of suffering an RRI than the IG after 12 months of follow up. Surely many factors contributed to this result, not only the IFM training. Predicting that the results would have influence of an unpredictable number of confounders, we did our best to ensure that both groups received the same monitoring, information and attention except for the specific interventions of each group. One way to minimize the effects of possible confounders is to simplify the method for strengthening the foot muscles, as reported by Ridge et al.(Ridge *et al.*, 2018), that managed to achieve an increase in IFM cross sectional area by just making the participants walk in minimal shoes with increased step count throughout the 8 weeks of study.

Another variable investigated in this study was the time elapsed until an injury occur (time to injury). Although the comparison of the average time-to-injury between groups showed no difference, there is not much validity in comparing the means since fewer subjects were injured in one of the groups. The most accurate way of determining time-to-injury is through logarithmic regression and estimating the time elapsed until a fixed percentage of the sample suffers an RRI. That was performed through quartile-estimation for 25% of RRI incidence. Although the usual comparison takes place at 50%, it would be too much of a stretch since total RRI incidence was 23.5%, resulting in large confidence intervals. Through this method, we found a significant difference in time to injury of 7.63±2.60 months for the control group and 10.15±2.69 months for the intervention group, demonstrating that the intervention group either had some resistance to injuries or the prevented injuries usually happen earlier than the ones observed in this group.

7.4 Strengths and Limitations

Strengths of the study include rigorous RCT methodology, inquiry about injury rates on a monthly basis rather than depending purely on injury incidence proportions, and a supervised training approach, which increased adherence to the protocol (88%) and reduced drop-out rates. In addition, this is the first study to evaluate RRI risk associated with a specific foot-training protocol focused on improving intrinsic foot-muscle strength for non-novice recreational long-distance runners.

Among the limitations of this study, the running assessment was performed while the participants were barefoot, a condition that they were not habituated (stablished in the inclusion criteria). This might have led to a larger variation of the running pattern and influenced the results for biomechanical variables.

The sample size was calculated using lower limb running related incidence for a chi-squared statistical model. The aim of simply performing a chi-squared test between the injury rate of the two groups at the end of the follow-up did not take into consideration that for a more complex survival analysis more subjects would have to participate the study. Even more if the idea was to enable an analysis discriminating types of injury with diagnostics or location of the pain such as Nielsen et al (Nielsen *et al.*, 2014) with 749 subjects.

Other limitation was sub-sampling the MRI exams. The costly nature of the tests and our restricted budget forced us to assess 50 participants, with only 28 completing the imaging at T0, T8 and T16 (without missing the assessment week or not getting injured at the first two months of study).

Although participants in the CG were not trained in the foot-core intervention, these runners were still receiving attention, and they were contacted if their weekly mileage was not reported. They were also reminded to contact the physiotherapist in case of any doubt, pain, or RRI, even if they did not think that the issue, they were experiencing matched the RRI definition we used. So, we believe that if the participants changed their natural behavior of running because they knew they were being observed, we may assume they did so similarly in both groups, diluting a possible Hawthorn effect.

7.5 Clinical Implications

Overall, we can affirm that the developed protocol is beneficial for runners and can be easily applied by running groups and coaches during training. The "bottom-up" approach was proven a valid way to influence running biomechanics even in its simpler aspect, without resorting yet to gait and running postural retraining.

We expected that, if any injury prevention was to be achieved, the intervention would prevent injuries near the foot region and surprisingly, there was no knee injuries reported in the IG. It is possible to speculate that the stresses dissipated by a trained foot/ankle complex may be somehow specifically harmful to the knee joint. Unfortunately, we did not have enough subjects to conduct an analysis differentiating types of injury.

The developed exercising protocol and its hereby shown implications on the injury incidence in runners goes against what is commonly believed to be the best approach on preventing running related injuries (Saragiotto, Yamato and Lopes, 2014; Wilke, Vogel and Vogt, 2019; Hofstede *et al.*, 2020).

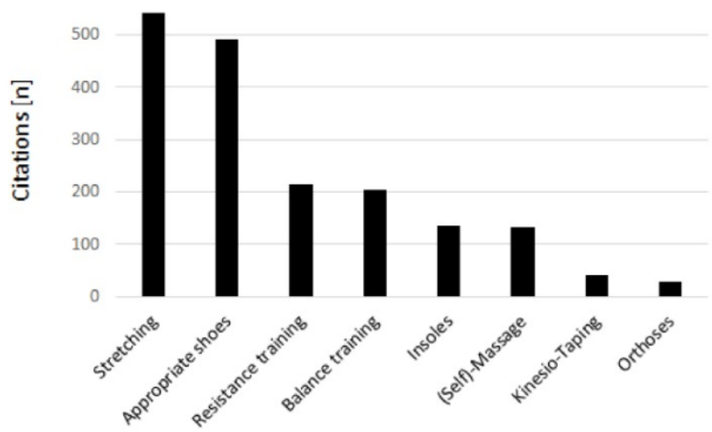


Figure 2- Practices that runners believe to be the best to prevent injuries during a race. Taken from Hofstede et al.(Hofstede *et al.*, 2020)

Previous belief is also related to the thinking that enhancing the proximal joints' muscles strength would prevent overall injuries in a theory that they are caused by reduced proximal (core) strength (Hott *et al.*, 2015) and, even though not proven to be efficient in preventing running related injuries, it is the strongly recommended by coaches in general. This is the conventional top-down approach to control joint movements that would be associated with injuries.

To our knowledge, this is the first time the bottom-up approach has proven to be so successful on altering running biomechanics and injury incidence in recreational long-distance runners.

8 CONCLUSION

The proposed clinical trial was feasible, since (i) recreational runners were willing to participate in the research, (ii) shared their information consistently throughout the research follow up, and (iii) had good adherence to the protocol. Furthermore, previous sample size estimation had proven to be sufficient for the variables of interest.

The foot core exercising protocol and the bottom-up approach proposed not only was effective in enhancing plantar muscles volumes, but also influenced running mechanics, increasing vertical impulse at the push-off phase.

The exercises program for foot core proposed decreased the incidence of RRIs with a 2.42 fold in recreational long-distance runners. This foot-exercise program showed evidence of effective RRI risk reduction in recreational runners at just 4-8 months of training. Although the mechanisms underlying the observed reduction in RRIs are uncertain, future studies with larger sample sizes would allow for better elucidation of causalities through the opportunity to stratify the survival analysis by injury type or site. Inclusion of different populations of runners, biomechanical factors, musculoskeletal factors, and a longer follow-up time might provide more insights on subgroups for which the intervention is more beneficial and specific risk factors influencing the survival analysis.

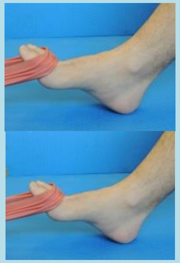
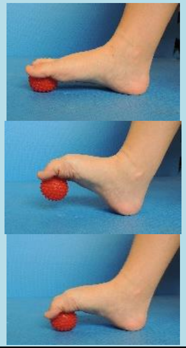
ANNEX 1 – FOOT CORE EXERCISES PROGRAM

Table 1 - Exercises included in the supervised sessions by a physiotherapist.

Name	Execution	Training Volume	Progression	Progression Parameter	Approximate Duration
Massage 	Sitting, with leg crossed over the other, massage the sole of your feet with both hands, for 20 seconds. Rub your foot in a circular motion using your thumb. Do the same on the other foot.	1 set of 20 seconds each foot	-	-	40 Seconds
Toes manipulation 	Sitting, with leg crossed over the other, hold each toe and slowly spin side to side, like a screw. Do with all toes.	1 set of 10 times each finger	-	-	1 minute

Rubber ball slide 	Slowly slide your foot on the ball throughout the foot sole from the heel to the fingertips.	1 set of 30 seconds each foot	-	-	1 minute
Feet tapping  	With the heel fixed, tap your foot as fast as possible. Starts seated on a chair, and do with both feet at the same time. After you learn, do the same tapping standing.	1 set of 30 repetitions	1: 1x30 repetitions; 2: 2x30 repetitions; 3: 2x40 repetitions	Being able to perform the set without pain or muscle cramp after the completion of the set.	1-2 minutes
Forefoot ascend 	Standing, ascend and descend on forefoot. Start standing, using both feet. Use a chair or table to keep balance.	1 set of 30 repetitions	1: 1x30 repetitions; 2: 2x30 repetitions; 3: 2x40 repetitions	Being able to perform the set without pain or muscle cramp after the completion of the set.	1-2 minutes

Invert/Evert asymmetric 	Sitting, with 90 degrees of knee and ankle flexion, perform asymmetrical foot inversion (lifting medial side) and eversion (lifting lateral side).	1 set of 10 repetitions maintaining each position for 1 second.	1: Sitting: 1x10 repetitions; 2: Standing: 1x10 repetitions ; 3: Standing 1x20 repetitions maintaining each position for 2 seconds.	Being able to perform the set without pain or muscle cramp after the completion of the set, and without loss of balance.	1-2 minutes
Foot abduction 	Standing, using a resistance band around the forefoot, perform foot abduction and return to the original position	2 sets of 10 repetitions each foot	1: 2x10 repetitions; 2: 4x10 repetitions; 3: 6x10 repetitions.	Being able to perform the set without pain or muscle cramp after the completion of the set.	1-6 minutes

Toes and ankle flexion 	Sitting posture, using a resistance band around the forefoot, perform ankle and toes flexion and return to the original position	1 sets of 10 repetitions each foot	1: 1x10 repetitions; 2: 2x10 repetitions; 3: 3x10 repetitions.	Being able to perform the set without pain or muscle cramp after the completion of the set.	1-3 minutes
Grab and hold squeeze ball 	Grab and hold a squeeze ball with all the toes, raise it from the floor and place it back to it's original position. Always keep the heel fixed on the ground.	1 sets of 5 repetitions each foot holding the ball for 5 seconds	1: Sitting posture 1x5 repetitions; 2: Standing posture 2x5 repetitions; 3: Standing posture 3x5 repetitions.	Being able to perform the set without pain or muscle cramp after the completion of the set.	2-6 minutes

Squeeze toes separators 	Sitting position, with 90 degrees of knee and ankle flexion, adduct and abduct, squeeze the toes separators for one second always keeping the heel fixed on the ground.	1 sets of 10 repetitions each foot	1: 1x10 repetitions; 2: 2x10 repetitions; 3: 3x10 repetitions.	Being able to perform the set without pain or muscle cramp after the completion of the set.	2-6 minutes
Squeeze ball with little toes 	Grab and hold a squeeze ball with the metatarsophalangeal region and place it back to the starting position.	1 sets of 5 repetitions each foot holding the ball for 5 seconds	Progression requires raising squeeze balls hardness.	Being able to perform the set without pain or muscle cramp after the completion of the set and being able to hold abduction for the stipulated time.	2 minutes

Toes Abduction/adduction 	Sitting position, with 90 degrees of knee and ankle flexion, adduct and abduct toes holding each position for 2 seconds.	1 sets of 10 repetitions each foot holding abduction for 2 seconds and adduction for 2 seconds.	1: Sitting posture 1x10 repetitions; 2: Standing posture 2x10 repetitions; 3: Standing posture 2x10 repetitions holding abduction/abduction for 5 seconds.	Being able to perform the set without pain or muscle cramp after the completion of the set and being able to hold abduction for the stipulated time.	1-2 minutes
Short-foot exercise 	Sitting, with 90 degrees of knee and ankle flexion, approximate the head of the first metatarsal toward the heel without toe flexion, “shortening” the feet. The forefoot and heel should not get off the ground.	1 set of 10 repetitions each foot, maintainin g 5 seconds each contractio n.	1: Sitting 1x10 repetitions; 2: Standing 1x10 repetitions; 3: Single leg stance 1x10 repetitions.	Being able to perform the set without pain or muscle cramp after the completion of the set.	4-6 minutes

Plantar arch raise 	Sitting, raise the plantar arch in an arch shape. The heel and fingertips should not get off the ground.	1 set of 10 repetitions each foot, maintaining 5 seconds each contraction.	1: Sitting 1x10 repetitions; 2: Standing 1x10 repetitions; 3: Single leg stance 1x10 repetitions.	Being able to perform the set without pain or muscle cramp after the completion of the set.	4-6 minutes

Table 2 – Exercises included in the remotely supervised sessions in the web software.

Name	Execution	Training Volume	Progression	Progression Parameter	Approximate Duration
Massage 	Sitting, with leg crossed over the other, massage the sole of your feet with both hands, for 20 seconds. Rub your foot in a circular motion using your thumb. Do the same on the other foot.	1 set of 20 seconds each foot	-	-	40 seconds

Toes manipulation 	Sitting, with leg crossed over the other, hold each toe and slowly spin side to side, like a screw. Do with all toes.	1 set of 10 times each finger	-	-	1 minute
Feet tapping 	With the heel fixed, tap your foot as fast as possible. Starts seated on a chair, and do with both feet at the same time. After you learn, do the same tapping standing.	1 set of 30 repetitions	1: 1x30 repetitions; 2: 2x30 repetitions; 3: 2x40 repetitions ;	Being able to perform the set without pain or muscle cramp after the completion of the set.	1-2 minutes

Forefoot accend 	Standing, ascend and descend on forefoot. Start standing, using both feet. Use a chair or table to keep balance.	1 set of 30 repetitions	1: 1x30 repetitions; 2: 2x30 repetitions; 3: 2x40 repetitions	Being able to perform the set without pain or muscle cramp after the fulfillment.	1-2 minutes
Invert/Evert symetric 	Sitting, with 90 degrees of knee and ankle flexion, perform symmetrical foot inversion (lifting medial side) and eversion (lifting lateral side).	1 set of 10 repetitions maintaining each position for 1 second.	1: Sitting 1x10 repetitions; 2: Standing 1x10 repetitions 3: Standing 1x20 repetitions	Being able to perform the set without pain or muscle cramp after the completion of the set and without loss of balance.	1-2 minutes

Cotton ball grab  **Rubber ball grab**  **Pen grab** 	While sitting, with the heel in a fixed position, grip the object with the toes, lifting off from the ground and placing it back to its original position. Do the same with the other foot.	1 set of 10 repetitions each foot.	1: 1x10 repetitions with cotton ball; 2:2x10 repetitions with rubber ball; 3: 3x10 repetitions with a pen.	Being able to perform the set without pain or muscle cramp after the completion of the set	3-6 minutes

1-5 toe alternate 	Sitting, with the heel fixed and contacting the floor, alternately pull the hallux and the little toe on the floor. Do it slowly and under complete control.	1 set of 10 repetitions each foot, maintaining finger pressure on the ground for 1 second.	1: Sitting 1x10 repetitions; 2: Standing 1x10 repetitions; 3: Single leg stance 1x10 repetitions.	Being able to perform the set without pain or muscle cramp after the completion of the set and with high control of speed and motion.	2-3 minutes
Toes abduction 	Sitting, with 90 degrees of knee and ankle flexion, abduct and adduct the toes rhythmically.	1 set of 10 repetitions each foot, maintaining 2 seconds abducted and 2 seconds on adducted.	1: Sitting 1x10 repetitions; 2: Standing 2x10 repetitions; 3: Standing 2x10 repetitions maintained for 5 seconds	Being able to perform the set without pain or muscle cramp after the completion of the set and be able to keep the abduction and adduction time.	1-2 minutes

Plantar arch raise 	Sitting, raise the plantar arch in an arch shape. The heel and fingertips should not get off the ground.	1 set of 10 repetitions each foot, maintaining 5 seconds each contraction.	1: Sitting 1x10 repetitions; 2: Standing 1x10 repetitions; 3: Single leg stance 1x10 repetitions.	Being able to perform the set without pain or muscle cramp after the completion of the set.	4-6 minutes
Short-foot exercise  	Sitting, with 90 degrees of knee and ankle flexion, approximate the head of the first metatarsal toward the heel without toe flexion, “shortening” the feet. The forefoot and heel should not get off the ground.	1 set of 10 repetitions each foot, maintaining 5 seconds each contraction.	1: Sitting 1x10 repetitions; 2: Standing 1x10 repetitions; 3: Single leg stance 1x10 repetitions.	Being able to perform the set without pain or muscle cramp after the completion of the set.	4-6 minutes
Toes grasping gait 	Walking “grasping” the toes when they touch the ground. Each step grasp for 3 seconds.	1 set of 10 steps.	1: 1x10 steps; 2: 2x10 steps; 3: 3x10 steps;	Being able to perform the set in the time described and without pain or muscle cramp after the completion of the set.	1-3 minutes
Toes abducted gait	Walking abducting the toes when the foot touches the ground until take the foot off the ground.	1 set of 3 steps forward and 3 steps backwards.	1: 1x10 repetitions; 2: 2x10 repetitions;	Being able to perform the set without pain or muscle cramp after the completion of the set.	2-6 minutes

			3: 3x10 repetitions;		

Table S3 – Warm up and stretching exercises.

Name	Execution	Training Volume	Approximate Duration
Calf stretch 	Standing in front of a wall, keep one leg in front of the other. The front leg with the knee flexed and the rear leg with the knee extended. Lean forward at the ankle, keeping both heel on the ground, stretching the calf muscles.	1 set of 20 seconds each leg.	40 seconds
Quadriceps stretch 	Standing on one foot, pull the heel towards the bottom, stretching the anterior muscles of the thigh. If necessary, use a wall for support.	1 set of 20 seconds each leg.	40 seconds

Fingertip-to-floor 	Standing, with your back straight, bend your trunk forward, keeping the knee straight, trying to touch the fingertip to the ground.	1 set of 20 seconds each leg.	40 seconds
Lateral stretch (1) 	Standing, with the back straight and with leg crossed over the other, bend the trunk forward, keeping both knees straight, trying to touch the fingertip to the ground.	1 set of 20 seconds each leg.	40 seconds

Adductors stretch 	Sitting, with back straight, knees apart and the sole of feet together, apply gentle pressure to your knees directed to the floor.	1 set of 20 seconds each leg.	40 seconds
Pretzel Stretch 	Lying, with leg crossed over the other, interlace your fingers on the back of the thigh, pulling the leg crossed towards the trunk.	1 set of 20 seconds each leg.	40 seconds
Lateral stretch (2) 	Lying with open arms, flex and adduct the hip directing the knee to the hand of the opposite side.	1 set of 20 seconds each leg.	40 seconds

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APPENDIX - ETHICS COMMITEE APPROVAL

MEDICINA

USP

COMITÊ DE ÉTICA EM PESQUISA

APROVAÇÃO

O Comitê de Ética em Pesquisa da Faculdade de Medicina da Universidade de São Paulo, em sessão de 18/03/2015, **APROVOU** o Protocolo de Pesquisa nº **031/15** intitulado: **"EFEITOS DO TREINAMENTO DA MUSCULATURA DO PÉ NA PREVALÊNCIA DE LESÕES EM CORREDORES FUNDISTAS: UM ENSAIO CLÍNICO CONTROLADO E RANDOMIZADO"** apresentado pelo **Departamento de FISIOTERAPIA, FONOAUDIOLOGIA E TERAPIA OCUPACIONAL**

Cabe ao pesquisador elaborar e apresentar ao CEP-FMUSP, os relatórios parciais e final sobre a pesquisa (Resolução do Conselho Nacional de Saúde nº 466/12, inciso IX.2, letra "c").

Pesquisador (a) Responsável: Isabel de Camargo Neves Sacco
Pesquisador (a) Executante: Ulisses Taddei Tirollo
Pesquisador (a) Executante: Alessandra Bento Matias

CEP-FMUSP, 18 de Março de 2015.

Prof. Dr. Roger Chammas
Coordenador
Comitê de Ética em Pesquisa