ARTIGO ORIGINAL

HIGH-INTENSITY STRENGTH TRAINING IN AN OLDER POPULATION: A PRELIMINARY STUDY

Treinamento de força de alta intensidade em uma população idosa: um estudo preliminar

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BACKGROUND: Osteoarthritis is the most common joint disease worldwide, and it occurs mainly later in life. Many factors are associated with osteoarthritis development, including decline in muscle strength. Muscle strengthening exercises have been recognized as important approaches to osteoarthritis conservative management of the knee; however, issues related to its applicability in terms of intensity are still elusive. **OBJECTIVE:** Studies using high-intensity exercises have shown inconsistent results, thus the purpose of this study was to analyze the response to high-intensity strength training for muscle strength and physical function in an older healthy population, as well as their attitudes towards the strength training. **METHODS**: This study employed a within-subject, repeated measure, in an experimental design to assess the response to strength training for physical mobility and strength in a cohort of 10 healthy older subjects at baseline and after six weeks of intervention. **RESULTS**: The statistical analysis demonstrated that knee extensor isokinetic peak torque significantly improved (p < 0.05) after intervention, whereas knee flexors only showed a trend for improvement (p = 0.066). Repetition maximum tests had significant improvements for all exercises performed. There was no change in physical mobility after intervention (p = 0.163). **CONCLUSION**: The results of this study demonstrate that high-intensity strength training was safe and has potential value in healthy older people. **KEYWORDS**: resistance training; aging; exercise.

INTRODUÇÃO: A osteoartrite é a doença articular mais comum em todo o mundo, e ocorre principalmente na vida adulta. Muitos fatores estão relacionados com o desenvolvimento da osteoartrite, incluindo diminuição da força muscular. Exercícios de fortalecimento muscular têm sido reconhecidos como importantes abordagens para o tratamento conservador da osteoartrite do joelho; no entanto, as questões relacionadas com a sua aplicabilidade, em termos de intensidade, ainda são inconclusivas. **OBJETIVO**: Estudos utilizando exercícios de alta intensidade mostram resultados controversos; assim, o objetivo deste estudo foi analisar a resposta à alta intensidade do treinamento de força para a força muscular e a função física em uma população mais idosa saudável, bem como as suas atitudes em relação a este treinamento de força. **MÉTODOS**: Este estudo utilizou uma única medida repetida de um sujeito, em um delineamento experimental, para avaliar a resposta ao treinamento de força para a mobilidade física e a força em uma coorte de 10 idosos saudáveis no início do estudo e após seis semanas do período de intervenção. **RESULTADOS**: A análise estatística mostrou que o torque isocinético dos músculos extensores do joelho apresentou melhora significativa (p < 0,005) após a intervenção, enquanto flexores do joelho mostraram apenas uma tendência de melhora (p = 0,066). Os testes de repetições máximas mostraram melhorias significativas para todos os exercícios realizados. Não houve alteração na mobilidade física após a intervenção (p = 0,163). **CONCLUSÃO**: Os resultados deste estudo demonstram que o treinamento de força de alta intensidade foi seguro e benéfico para indivíduos idosos saudáveis.

PALAVRAS-CHAVE: treinamento de resistência; envelhecimento; exercício.

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BSTRACT

INTRODUCTION

Osteoarthritis (OA) is a chronic joint disease and the leading cause of musculoskeletal pain and disability. The knee joint is more commonly affected,¹ and based on current trends, it has been estimated that over 26 million people in the USA have some kind of OA.^{2,3}

Many factors are associated with the development of osteoarthritis including age, sex, ethnicity, race⁴ and ageing,⁵ possibly due to the many age-related musculoskeletal factors like decline in muscle strength.⁶

Since muscle weakness, pain and physical dysfunction form a vicious cycle in the OA knee, muscle strengthening exercises have been recognized as the cornerstones of conservative management.^{4,7} However, many factors related to its applicability in terms of dosage still need to be clarified. For instance, even though high-resistance strength training is expected to promote greater strength gain, studies have shown that its effects are not always greater than those of low-resistance strength training in patients with OA knee.^{7,8} Furthermore, despite the uncertainty over the ideal intensity to be employed, there is concern as to whether these benefits would be translated into substantive clinical outcomes, such as greater pain relief and functional performance, and if this intensity would have a detrimental effect to the joints.

Since there are very few studies⁸⁻¹⁰ published using high-intensity strength training in patients with OA, and many are of limited quality in methodological terms, the purpose of this study was twofold: to analyze the response to high-intensity strength training for muscle strength and physical function in an older healthy population, and to investigate the attitudes of participants towards the strength training particularly designed for this study. If tolerance were demonstrated in these healthy older adults, a future study could be developed to evaluate tolerability in OA subjects.

METHODS

Patient selection

A cohort of 10 healthy, sedentary subjects aged over 60 years were recruited through advertisements in the School of Health Care Science of Cardiff University's newsletter and via the Internet. After obtaining the informed consent from all subjects, they were enrolled in the study between October and December 2013. Subjects were excluded if current complaints were presented from lower limb or back pain, chronic knee pain, or any medical condition that would prevent subjects from taking part in the strength training. No evidence of OA was found in subjects enrolled in the study.

Study design

A within subject, repeated measures, experimental design was used to assess the response to strength training for physical mobility and strength at baseline and after six weeks of intervention. An investigation of possible barriers, enablers and attitudes towards high-intensity strength exercises was also conducted. A pilot study with two independent subjects was first conducted, in order to confirm feasibility and to explore possible adverse events (pain, discomfort, muscle soreness etc.), from the protocol of exercises, assuming the same conditions as the planned study. The draft questionnaire designed to gain insight into attitudes, barriers and enablers to exercise was also applied to these two subjects.

The ethical evaluation and approval of the full experimental procedures protocol was undertaken by the School of Health Care Research Committee of Cardiff University.

Intervention

Volunteers were given individual time slots according to preference. Visits lasted on average 45 minutes to one hour, three times a week, over a period of six weeks. All volunteers were submitted to the same procedures, in the same order as presented in the training protocol. They started all exercise sessions by warming up on a stationary bicycle for five minutes followed by dynamic stretches of upper and lower limb muscle groups. They were subsequently introduced to pieces of equipment. Volunteers were required to perform three sets of six repetitions of exercise when possible and had a two-minute rest between each set of exercise. On the first two sessions, all volunteers performed three sets of six repetitions at an initial percentage of 70% of a one-repetition maximum (1 RM) of the five exercises: squats, lunges, leg press, leg extension, and leg curls. The progression within the program was based on whether the participant could perform two extra repetitions for the given exercise in two consecutive training sessions¹¹. If the participants were able to perform them, the training load would be increased on the next training session by 5 to 10%, depending on the physical capacity and adaptability to the exercises.

Data collection

Isokinetic muscle strength testing

The isokinetic muscle strength assessment, in which reliability was established,¹² was conducted using a Kin-Com dynamometer (Chattecx Corp, Hixon, the USA) at the Research Centre for Clinical Kinesiology of Cardiff University. The test was carried out using knee extensors and flexors muscles at a velocity of 90°/s and three attempts for each muscle

group were taken through concentric isokinetic assessment. For analysis purposes, the average of three measures was calculated for each muscle group.

Adherence to the strength training intervention was calculated based on workout logs filled out by researchers that were reviewed weekly. In order to calculate the overall adherence, the total number of workout sessions performed was divided by the total amount of possible sessions.

Repetition maximum testing

Following a warm-up, individuals then chose a load that they believed they could lift for six repetitions in five different exercises — squats, lunges, leg press, leg extension, and leg curls. If a subject was able to perform more than six repetitions with this load, he/she stopped and rested for two minutes. A five-minute rest between each type of exercise was also employed. Depending on subject's perceived level of exertion, the load was then increased by 10 to 20%¹² and the test was repeated. When required, this process was continued until a maximum load was reached that restricted the subject to six repetitions or less, as in the literature.¹² The initial load for training was then calculated as 70% of estimated RM, using a table based on prediction equations.¹³

Timed Up and Go

The test was performed by measuring the time in seconds for a person to rise from sitting on a standard armchair, walk three meters, turn, walk back to the chair, and sit down. For the test, the individual was required to wear regular footwear.¹⁴

Attitudes, enablers and barriers towards the exercise questionnaire

A questionnaire with 10 questions based on a five-point Likert scale and two open-ended questions was designed. On the first set of questions, volunteers were asked about their feelings towards the exercises, its overall impact on their physical health, their opinion on the positive aspects of the program, as well as what could have been done to improve the quality of the exercise program. On the second block of questions, emphasis was placed on the general features of the program exercises, such as the frequency, types and volume of exercise performed, and equipment and assistance provided, as well as the progression of the exercises. The questionnaire was administered at the end of the last session of exercises.

Statistical analysis

Descriptive data for the Timed Up and Go, isokinetic muscle force, and 1 RM measures was recorded and tested for normal distribution. Statistical analysis was performed through comparison of means obtained from a paired *t*-test for data presenting normal distribution (as assessed through Shapiro-Wilk test), or a non-parametric test of Wilcoxon for data with non-normal distribution. An alpha level of 0.05 was used. Due to the small sample size, results with a p-value < 0.1 were taken as a trend. Statistical analysis was conducted using IBM SPSS version 20 for Mac (IBM Corp., Armonk, NY, USA).

RESULTS

Ten healthy older adults (8 females and 2 males) composed the sample used for his study, with an average of 60.7 years. The compliance rate was 90% as one subject dropped out of the study. Many of the subjects were unable to adhere to the requested attendance for training, so the overall adherence was 62%, with an average of 7.8 sessions attended per subject.

Table 1 presents the means and standard deviation values for isokinetic peak muscle force, at baseline and after intervention. Only knee extensor muscles presented a significant improvement (p < 0.05).

In Table 2, all five exercises used for the RM testing presented statistically significant post-intervention improvements: squats, lunges, leg press, leg extension and

Table	1	Means	and	stand	dard	devia	ation	baselir	ie	and
post-in	ite	rventior	for i	sokine	etic p	eak fo	rce of	^F knee m	lus	cles

Muscle group		Baseline	Post-intervention	p-value*		
	Flexors	248.9 N ± 86.4	258 N ± 68.5	0.066		
	Extensors	355.9 N ± 117.4	438 N ± 62.0	0.042		

Isokinetic peak muscle force expressed in Newton (N). *Paired t-test.

Table 2 Pre and post-intervention values for one repetition	ſ
maximum by exercise type	

Fuercies	Pre intervention	Post-intervention	p-value	
Exercise	Mean ± SD*	Mean ± SD*		
Squats	23.38 ± 20.86	36 ± 20.51	0.013	
Leg press	95.25 ± 24.24	122.38 ± 27.07	0.023	
Leg extension	19.38 ± 7.44	21.75 ± 6.84	0.035	
	Median**	Median**		
Leg curls	8.0	11.0	0.045	
Lunges	5.5	10.5	0.008	

SD: standard deviation; *paired *t*-test; **non-parametric Wilcoxon rank signed test.

leg curls. Although knee flexors isokinetic peak torque showed only a trend for improvement (p = 0.066), 1 RM values for leg curls (exercise for the hamstrings muscles) achieved statistical significance.

Table 3 displays Timed Up and Go scores pre and post-intervention. A non-parametric test of Wilcoxon was used due to abnormal distribution of data. Difference between baseline and post-intervention scores was not statistically significant (p = 0.163).

Attitudes, enablers and barriers towards exercise questionnaire

Table 4 shows the responses for each question. Nearly all volunteers presented a positive approach towards the exercises when asked about the benefits of the program and most believed that exercises with weights would be potentially helpful to keep their joints healthy. However, only half of them stated they would definitely carry on with the exercises. About the use of exercises performed for future management of people suffering from OA, most were unsure whether this set of exercises would be helpful.

Table 5 displays the ratings for the second block of questions in which emphasis was given to features of the strength training itself, such as the type of exercises performed and equipment provided.

The majority of volunteers found the exercises chosen for this program to be suitable to perform and rated the progression as varying between good to very good. Other features also

 Table 3 Pre and post-intervention values for Timed Up and

 Go test scores*

	Timed up and Go test				
	Pre-intervention	Post-intervention			
Median	5.44	5.10			
Means	5.38	5.15			
Standard deviation	± 0.56	± 0.53			

*scores are presented in seconds (s).

Table 4 Responses to Block 1 questions

presented a positive rating (volume, supervision, equipment and duration), with no negative ratings being recorded.

Points mentioned by volunteers that may be seen as potential barriers to exercise were pieces of equipment used (three volunteers indicated that using the barbell to perform squat exercise might be harmful to their back), and order of the exercises performed (three mentioned that altering the order of the exercise would improve the quality of their training). As a response when asked about possible suggestions to increase quality of the program, comments were made about the lack of social interaction with their peers.

DISCUSSION

Effects of high-intensity strength training on muscle force

A significant improvement was observed on muscle force after subjects performed strength training, as shown in the results of 1 RM test for each one of the exercises performed, both emphasizing the knee extensors (lunges, squats, leg press and leg extension) and knee flexors (leg curls) muscles.

Kryger and Andersen¹⁵ using a similar program design showed that, after 12 weeks of heavy resistance training (80% of 1 RM), elderly subjects had their isokinetic knee extensor strength increased by 41%. Significant strength gains after intervention were also shown through the 1 RM values, such as increased values for squats (56.52%), lunges (90.9%), leg press (34.94%), leg extension (12.27%), and leg curls (37,5%). Other studies^{16,17} using high-intensity exercises have also revealed significant strength gains in RM tests. For example, Hagerman et al.¹⁶ showed increases of 1 RM strength from pre-training values for leg extension (50.4%), for leg press (72.3%), and for half squat (83.5%). In agreement with our study results, these studies highlight the safety of this training modality if performed with caution, presented with

Question	Agree	Somewhat Agree	Neutral	Somewhat disagree	Disagree
1. This exercise programme has been of great benefit to me personally.	4	5	0	1	0
2. Exercise programmes using weights like this one will help maintain healthy joints.	5	2	3	0	0
3. High-Intensity Strength Training is potentially useful in the management of lower limb joint conditions such as ostheoarthritis.	1	1	7	1	0
4. I will definitely carry on with this high-intensity strength training like this.	5	1	2	1	1

Questions	Very good	Good	Okay	Poor	Very poor
1. The type of exercises used.	2	8	0	0	0
2. The volume of exercises.	2	3	5	0	0
3. The way in which the exercises were progressed.	2	6	2	0	0
4. The support and supervision offered by the therapist.	8	2	0	0	0
5. The equipment used for training.	5	3	2	0	0
6. The duration of sessions.	3	5	2	0	0

Table 5 Responses to Block 2 questions

a carefully designed structure as well as ongoing monitoring of the subjects involved.

Results that seem conflicting were found between significant improvements to leg curls in 1 RM values and absence of improvements to isokinetic knee flexor strength. However, these two techniques might not be in agreement when it comes to muscle strength proportion, that is, one of the techniques could show more remarkable gains when compared to the other. Additionally, the 1 RM technique used in previous studies differs from the technique used in the current study, whose values were predicted after subjects had performed multiple RM testing. Hence, the increase in 1 RM value for the leg curls in the present study may not be due completely to strength training.

Strength gains in this study may well be attributed to some sort of neuromuscular adaptation, as suggested by Baechle et al.¹³ who affirmed that much of the improvement in strength evidenced in the first few weeks of resistance training is attributed to neural adaptations. Moreover, it could be deemed that the strength training regimen performed by the volunteers in this study avoided undesirable events that were not reported in many other studies,¹⁸⁻²³ and was also efficient for leading subjects to begin building up substantial muscle strength.

Effects of high-intensity strength training on physical mobility

Even though strength gains were significant, such improvements were not translated into greater functional performance on Timed Up and Go (TUG). The baseline score of 5.38 seconds on the TUG test suggests good physical mobility according to the TUG normality scores,²⁴ and further improvement would have been challenging. Thus, it seems that a more sensitive mobility scale or another performance assessment would be more suitable to evaluate healthy older subjects in their early 60's. In a study that did show that strength training enhanced greater functional performance on the TUG test in healthy older subjects,²⁵ the participants had a higher baseline score and were older than the subjects in the current study. Based on the assumption that the older the subjects the more prone they are to develop muscles impairment,⁶ it seems that their subjects had a greater potential to show significant improvements after training.

In order to truly assess the impact of the strength training on physical mobility, further studies would need to include subjects with physical impairment that was reflected by the baseline values of TUG, or healthy older subjects who were considerably older than 60 years.²⁶

Attitudes, barriers and enablers towards high-intensity strength program

Nearly all the volunteers had a very positive approach towards exercises in relation to the benefits of the program for themselves. This is in line with the results obtained in a study conducted by Henwood et al.²⁷ in which the impact of resistance training, physical activity and exercise on general health was the most regularly mentioned concept, with all participants acknowledging that these training forms have important physical benefits.

The features of our exercise program followed the guidelines²⁸ and recommendations with regard to training frequency, number of sets and repetitions, rest periods and workload progression. Even though our subjects were not sure about recommending the exercises to people with joint conditions, they still considered the program safe. All volunteers rated the exercises used, the volume prescribed and their progression as being okay to very good, with no adverse comments.

It was mentioned by several volunteers that the set of exercises would possibly be more motivating if done with others in the same environment. In a recent paper²⁹ published on how to motivate older subjects to exercise, the element of social interaction was highlighted as being an important strategy not only to motivate older adults, but also to keep them motivated while engaged in a physical activity program. Thus, it seems that social interaction would be an important enabler to exercises since volunteers could share their experiences as well as ways of coping with them and benefits acquired from attending sessions.

Limitations

Even though it was a feasibility study, the small sample size used in the study was not enough to represent the entire population. Furthermore, blinding of assessments was not performed, which could induce biased results.

CONCLUSION

High-intensity strength training is an important intervention to increase muscle strength in older adults, and its clinical applicability appears to be safe. Strength gains, nevertheless, did not produce significant changes in participant's physical mobility, assessed by TUG. Subjects had a generally positive approach towards the training, recognizing they benefited from attending the program. Thus, the use of high-intensity strength training seems to be a safe and acceptable option to promote significant gains in healthy older subjects. Future studies in OA patients need to be developed to verify if similar clinical improvements can be made.

CONFLICT OF INTERESTS

The authors report no conflict of interests.

REFERENCES

- Haq SA, Davatchi F. Osteoarthritis of the knees in the COPCORD world. Int J Rheum Dis. 2011;14(1):122-9.
- Lawrence R, Felson DT, Helmick CG, Arnold LM, Choi H, Deyo RA, et al. Estimates of the prevalence of arthritis and other rheumatic conditions in the United States. Part II. Arthritis Rheum. 2008;58(1):26-35.
- Burbine SA, Weinstein AM, Reichmann WM, Rome BN, Collins JE, Katz JN, et al. Projecting the future public health impact of the trend toward earlier onset of knee osteoarthritis in the past 20 years. American College of Rheumatology Annual Scientific Meeting, Chicago; 2010.
- Litwic A, Edwards MH, Dennison EM, Cooper C. Epidemiology and burden of osteoarthritis. Br Med Bull. 2013;105:185-99.
- Loeser RF. Age-related changes in the musculoskeletal system and the development of osteoarthritis. Clin Geriatr Med. 2010;26(3):371-86.
- Narici MV, Maffulli N. Sarcopenia: characteristics, mechanisms and functional significance. Br Med Bull. 2010;95(1):139-59.
- Iwamoto J, Sato Y, Takeda T, Matsumoto H. Effectiveness of exercise for osteoarthritis of the knee: a review of the literature. World J Orthop. 2011;2(5):37-42.
- Jan MH, Lin JJ, Liau JJ, Lin YF, Lin DH. Investigation of clinical effects of high and low resistance training for patients with knee osteoarthritis: a randomized controlled trial. Phys Ther. 2008;88(4):427-36.
- King LK, Birmingham TB, Kean CO, Jones IC, Bryant DM, Giffin JR. Resistance training for medial compartment knee osteoarthritis and malalignment. Med Sci Sports Exerc. 2008;40(1):1376-84.
- Thorstensson CA, Roos EM, Petersson IF, Ekdahl C. Six weeks high-intensity exercise program for middle-aged patients with knee osteoarthritis: a randomized controlled trial. BMC Musculoskelet Disord. 2005;6(27):1-10.
- Feiring DC, Ellenbecker TS, Derscheid GL. Test-retest reliability of the biodex isokinetic dynamometer. J Orthop Sports Phys Ther. 1990;11(7):298-300.
- McNair PJ, Colvin M, Reid D. Predicting maximal strength of quadriceps from submaximal performance in individuals with knee joint osteoarthritis. Arthritis Care Res (Hoboken). 2011;63(2):216-22.
- Baechle T, Earle R, Wathen D. Resistance training. In: Baechle T, Earle R, eds. Essentials of strength training and conditioning. Champaign, IL: Human Kinetics; 2008. p. 381-412.
- Nordin E, Rosendahl E, Lundin-Olsson L. Timed "Up & Go" test: reliability in older people dependent in activities of daily living--focus on cognitive state. Phys Ther. 2006;86(5):646-55.
- Kryger AI, Andersen JL. Resistance training in the oldest old: consequences for muscle strength, fiber types, fiber size, and MHC isoforms. Scand J Med Sci Sports. 2007;17(4):422-30.

- Hagerman FC, Walsh SJ, Staron RS, Hikida RS, Gilders RM, Murray TF, et al. Effects of high-intensity resistance training on untrained older men. I. Strength, cardiovascular, and metabolic responses. J Gerontol A Biol Sci Med Sci. 2000;55(7):B336-46.
- Wood RH, Reyes R, Welsch MA, Favaloro-Sabatier J, Sabatier M, Matthew Lee C, et al. Concurrent cardiovascular and resistance training in healthy older adults. Med Sci Sports Exerc. 2001;33(10):1751-8.
- Fiatarone MA, Marks EC, Ryan ND, Meredith CN, Lipsitz LA, Evans WJ. High-intensity strength training in nonagenarians. JAMA. 1990;263(22):3029-34.
- Frontera WR, Meredith CN, O'Reilly KP, Knuttgen HG, Evans WJ. Strength conditioning in older men: skeletal muscle hypertrophy and improved function. J Appl Physiol (1985). 1988;64(3):1038-44.
- Häkkinen K, Häkkinen A. Neuromuscular adaptation during intensive strength training in middle aged and elderly males and females. Electromyogr Clin Neurophysiol. 1995;35(3):137-47.
- Häkkinen K, Pakarinen A, Kraemer WJ, Häkkinen A, Valkeinen H, Alen M. Selective muscle hypertrophy, changes in EMG and force, and serum hormones during strength training in older women. J Appl Physiol (1985). 2001;91(2):569-80.
- Reeves ND, Narici MV, Maganaris CN. Musculoskeletal adaptations to resistance training in old age. Man Ther. 2006;11(3):192-6.
- Vincent KR, Braith RW, Feldman RA, Magyari PM, Cutler RB, Persin SA, et al. Resistance exercise and physical performance in adults aged 60 to 83. J Am Geriatr Soc. 2002;50(6):1100-7.
- Podsiadlo D, Richardson S. The timed "Up & Go": a test of basic functional mobility for frail elderly persons. J Am Geriatr Soc. 1991;39(2):142-8.
- Mangione KK, Miller AH, Naughton IV. Cochrane review: improving physical function and performance with progressive resistance strength training in older adults. Phys Ther. 2010;90(12):1711-5.
- Peterson MD, Rhea MR, Sen A, Gordon PM. Resistance exercise for muscular strength in older adults: a meta-analysis. Ageing Res Rev. 2010;9(3):226–37.
- Henwood T, Tuckett A, Edelstein OE, Bartlett H. Exercise in later life: the older adults' perspective about resistance training. Ageing Soc. 2010;31(8):1330-49.
- American College of Sports Medicine, Chodzko-Zajko WJ, Proctor DN, Fiatarone Singh MA, Minson CT, Nigg CR, Salem GJ, Skinner JS. American College of Sports Medicine position stand. Exercise and physical activity for older adults. Med Sci Sports Exerc. 2009;41(7):1510-30.
- Bennett J, Winter-Stone K. Motivating older adults to exercise, what works? Age Ageing. 2011;40:148-9.