



## Maximum voluntary muscle contraction and fatigue in multibacillary leprosy

*Contração voluntária máxima e fadiga no paciente com hanseníase multibacilar*

*Contracción voluntaria máxima y fadiga en el paciente con hanseniasis multibacilar*

Luciane Lobato Sobral <sup>[a]</sup>, Marcio Clementino de Souza Santos <sup>[a]</sup>,  
Larissa Salgado de Oliveira Rocha <sup>[a,b]</sup>, Bianca Callegari <sup>[c]</sup>,  
Givago da Silva Souza <sup>[c]</sup>, Rosana Macher Teodori <sup>[d]\*</sup>

<sup>[a]</sup> Universidade do Estado do Pará (UEPA), Belém, PA, Brazil

<sup>[b]</sup> Centro Universitário do Estado do Pará (Cesupa), Belém, PA, Brazil

<sup>[c]</sup> Universidade Federal do Pará (UFPA), Belém, PA, Brazil

<sup>[d]</sup> Universidade Metodista de Piracicaba (Unimep), Piracicaba, SP, Brazil

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### Abstract

**Introduction:** The impairment of muscle strength and fatigue in leprosy remains a problem that requires careful attention to avoid or minimize its progression, as well as prevention of disabilities and deformities.

**Objective:** To investigate the maximum voluntary contraction and time to muscle fatigue in leprosy patients.

**Method:** A total of 21 leprosy patients and 21 healthy subjects completed the sample. The method used to determine the maximum voluntary contraction (MVC) of the handgrip followed the recommendation of the

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\* LLS: PhD, e-mail: [lucianelobatosobral@gmail.com](mailto:lucianelobatosobral@gmail.com)

MCSS: PhD, e-mail: [marcio.clementino@gmail.com](mailto:marcio.clementino@gmail.com)

LSOR: PhD, e-mail: [lari1980@gmail.com](mailto:lari1980@gmail.com)

BC: PhD, e-mail: [callegaribi@uol.com.br](mailto:callegaribi@uol.com.br)

GSS: PhD, e-mail: [givagosouza@gmail.com](mailto:givagosouza@gmail.com)

RMT: PhD, e-mail: [teodori@gmail.com](mailto:teodori@gmail.com)

American Society of Hand Therapists with the use of a hydraulic hand grip dynamometer. The test was performed three times with each hand, with a time interval of 60 seconds between successive trials. The subject was instructed to perform a maximal isometric force against the dynamometer for 5 seconds. The peaks were recorded and used for the fatigue test. For the fatigue test, we recorded the electromyogram of the forearm muscles to offline determine the onset time for the muscle contraction (14 bits, Miograph 2 USB®, Miotec, Brazil). **Results:** Leprosy patients had lower MVC compared with healthy subjects ( $p < 0.05$ ), both in the dominant and the non-dominant hands. The time to fatigue in the leprosy and control groups was similar ( $p > 0.05$ ). We observed that leprosy patients had more contractions than the healthy subjects ( $22.6 \pm 11.8$  contractions for the leprosy group vs.  $12.3 \pm 6.9$  contractions for the control group,  $p < 0.05$ ). **Conclusion:** Multibacillary leprosy patients lost muscle force without modifying the resistance to fatigue.

**Keywords:** Leprosy. Musculoskeletal System. Muscle Tonus. Muscle Fatigue. Muscle Strength.

## Resumo

**Introdução:** O comprometimento da força muscular e a fadiga na hanseníase continuam sendo problemas que requerem cuidadosa atenção para evitar ou minimizar sua progressão, bem como prevenir incapacidades e deformidades. **Objetivo:** Avaliar a força muscular e o tempo até a fadiga em pacientes com hanseníase. **Método:** Vinte e um pacientes com hanseníase e 21 indivíduos saudáveis completaram a amostra. O método utilizado para determinar a contração voluntária máxima (CVM) da força de preensão palmar seguiu a recomendação da Sociedade Americana de Terapeutas da Mão com o uso de um dinamômetro de preensão manual. O teste foi realizado três vezes em cada mão, com intervalo de tempo de sessenta segundos entre tentativas sucessivas. O sujeito foi instruído a realizar força isométrica máxima contra o dinamômetro durante cinco segundos. Os picos foram registrados e usados para o teste de fadiga. Para o teste de fadiga, registrou-se o eletromiograma dos músculos do antebraço para determinar off-line o tempo de início da contração muscular (14 bits, Miograph 2 USB®, Miotec, Brasil). **Resultados:** Os pacientes com hanseníase apresentaram menor CVM em relação aos saudáveis ( $p < 0,05$ ) nas mãos dominante e não dominante. Não houve diferença no tempo de fadiga entre os grupos hanseníase e controle ( $p > 0,05$ ). Foi observado que os pacientes com hanseníase tinham mais contrações do que os saudáveis ( $22,6 \pm 11,8$  contrações para o grupo com hanseníase vs.  $12,3 \pm 6,9$  para o grupo controle,  $p < 0,05$ ). **Conclusão:** Pacientes com hanseníase multibacilar apresentaram perda de força muscular sem modificação da resistência à fadiga.

**Palavras-chave:** Hanseníase. Sistema Musculoesquelético. Tono Muscular. Fadiga Muscular. Força Muscular.

## Resumen

**Introducción:** El compromiso de la fuerza muscular y la fatiga en la lepra sigue siendo un problema que requiere atención cuidadosa para evitar o minimizar su progresión, así como la prevención de incapacidades y deformidades. **Objetivo:** Evaluar la fuerza muscular y el tiempo hasta la fatiga de pacientes con lepra. **Método:** Veintiún pacientes con lepra y 21 sujetos sanos completaron la muestra. El método utilizado para determinar la contracción voluntaria máxima (CVM) de la fuerza de asimiento palmar siguió la recomendación de la Sociedad Americana de Terapeutas de la Mano con el uso de un dinamómetro de asimiento manual. La prueba se realizó tres veces con cada mano, con un intervalo de tiempo de 60 segundos entre intentos sucesivos. El sujeto fue instruido a realizar una fuerza isométrica máxima contra el dinamómetro durante 5 segundos. Los picos se registraron y se utilizaron para la prueba de fatiga. Para la prueba de fatiga, registramos el electromiograma de los músculos del antebrazo para determinar fuera de línea el tiempo de inicio de la contracción muscular (14 bits, Miograph 2 USB®, Miotec, Brasil). **Resultados:** Los pacientes con lepra presentaron menor CVM con relación a los sanos ( $p < 0,05$ ) en las manos dominante y no dominante. No hubo diferencia en el tiempo de fatiga entre los grupos de lepra y control ( $p > 0,05$ ). Se observó que los pacientes con lepra tenían más contracciones que los sanos ( $22,6 \pm 11,8$  contracciones para el grupo con hanseniasis frente a  $12,3 \pm 6,9$  para

*el grupo control,  $p < 0,05$ ). Conclusión: Pacientes con hanseniasis multibacilar presentaron pérdida de fuerza muscular sin modificación de la resistencia a la fatiga.*

**Palabras clave:** *Leprosia. Sistema Musculoesquelético. Tono Muscular. Fatiga Muscular. Fuerza Muscular.*

## Introduction

Leprosy is still a challenge for the public or private health systems in poor and developing countries, such as Brazil, India, and Indonesia [1]. It is an endemic disease that impairs the quality of life of those infected [2, 3]. Moreover, this disease brings a substantial financial burden every year for health systems to diagnose it, treat it, and rehabilitate the patients [4]. This infectious disease is caused by *Mycobacterium leprae*, which can damage the peripheral nerves and skin, resulting in physical disability and deficit in daily living activities [3, 5, 6]. Leprosy neuropathy is characterized by changes in somesthetic sensitivity, muscle weakness, muscle paralysis, deformities, and a decrease in limb functionality [7-9]. Furthermore, delay in the diagnosis and treatment of leprosy can lead to significant physical disabilities of patients [10].

Many authors have suggested several functional evaluations that could be used as an early predictor of neural changes in leprosy patients [11-13]. One of the possible targets for functional evaluation of leprosy patients is their hands. The leprotic hand is affected by the palsy of the ulnar, median and radial nerves [14]. Several deformities result from the nerve involvement, such as the claw hand [15]. A consequence of the onset of the hand deformities is power grip loss [16].

The hand grip strength has been associated with functional health [17], nutritional status [18] and whole-body muscle strength status [19]. The grip strength of the leprotic hand was a predictor of motor nerve impairment [9]. Few studies had investigated muscle fatigue in leprosy patients [20, 21]. Intermittent isometric hand grip contractions have been used to evaluate the forearm fatigue in health or disease conditions [22, 23]. Muscle fatigue is a strength reduction of the muscle induced by constant activity [24]. It has nervous and muscle components of its generation [25, 26]. The fatigue onset occurs with decline of the performance in executing a task, as well as with pain and discomfort

during the movement [27]. There are many reports on muscle weakness, but no clear information about muscle fatigue in leprosy patients. Thus, we aimed to evaluate muscle strength and fatigue in leprosy patients to compare with non-leprosy infected subjects to understand the possible mechanism of muscle involvement in this disease.

## Methods

### Subjects

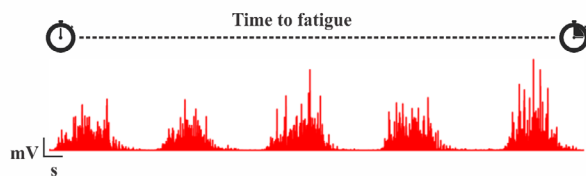
A total of 42 subjects were grouped in the control group (n = 21, 16 males, 5 females,  $36.2 \pm 12.6$ -year-old) and in the leprosy group (n = 21, 16 males, 5 females,  $39.1 \pm 10.6$ -year-old). All subjects were sedentary and had no history of systemic or neurological diseases; they were non-smoking people and had no deformities in the hand. All subjects gave the written consent to participate in the investigation, and the procedures were approved by the Human Research Ethics Committee of the Tropical Medicine Nucleus, Federal University of Pará (report #82226).

### Experimental procedures

We investigated the time to muscle fatigue in the hand-gripping task. First, we estimated the maximum voluntary contraction (MVC) of the hand grip. To this end, we followed the recommendation of the American Society of Hand Therapists [28]. A hydraulic hand grip dynamometer (SAEHAN corporation, SH5001 model, Korea) was used. The subjects sat upright in a chair, with the plantar surface of the feet touching the ground, hips and knees flexed at  $90^\circ$ , shoulders fully adducted, elbow flexed at  $90^\circ$ , forearms and wrist at  $0^\circ$ . The subject sustained the dynamometer with one hand while the untested hand rested. The test was performed three times with each hand with a time interval of 60 s between successive trials. The subject was instructed to perform a maximal isometric force against the dynamometer for 5 s.

The peaks were recorded, the hand with higher mean muscle strength was considered as dominant and was used for the fatigue test. For the fatigue test, we recorded the electromyogram of the forearm muscles using electromyographer to offline determine the onset time of the muscle contraction (14 bits, Miograph 2 USB®, Miotec, Brazil). Before the electrodes' placement, we removed the hairs on the skin and cleaned the area with soap. 1 cm-silver-chloride (Ag-AgCl) circular surface electrodes were connected to electromyography (EMG) sensors (SDS500) and placed in the flexor digitorum superficialis muscle following the recommendations of the SENIAM project (surface electromyography for non-invasive assessment of muscles). The electrodes were placed in the muscle belly with an interelectrode center-to-center distance of 2 cm.

EMG signals were amplified 100× with a frequency window between 0.1 Hz and 1000 Hz and digitized at 2 KHz. The EMG recording started when the subject started the muscle contraction of the hand grip. We instructed the subjects to intermittently grasp the dynamometer with the maximum force they could, with no specific frequency of contraction. The recording stopped when the force applied during the hand grip task reached 70% of the MVC. Figure 1 shows a scheme of the fatigue test. Each subject performed one trial of the fatigue test. We counted the number of EMG contractions during the time to fatigue.



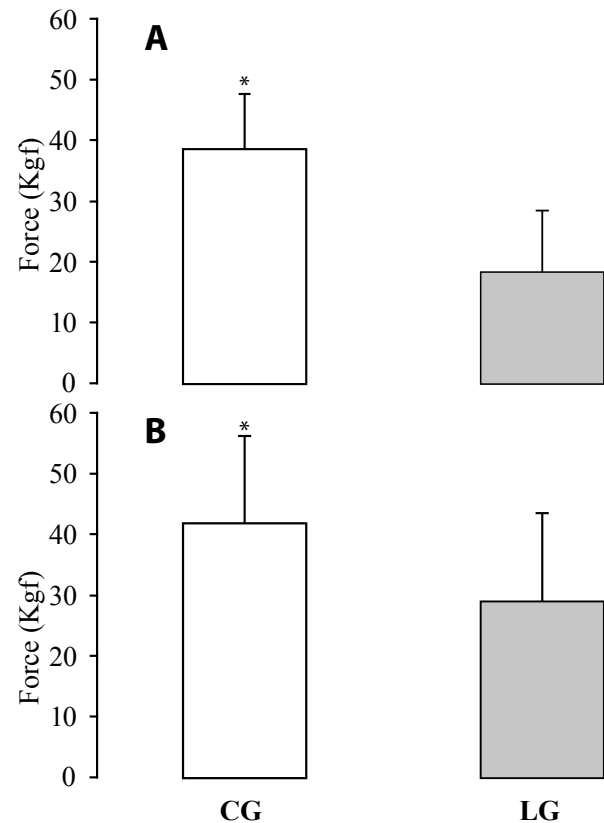
Note: Time to fatigue was the duration of the sequence of muscle contractions above 70% of the maximum voluntary contraction. The number of contractions during the fatigue test was counted using electromyography (EMG) information.

**Figure 1** – Scheme of the fatigue test.

## Results

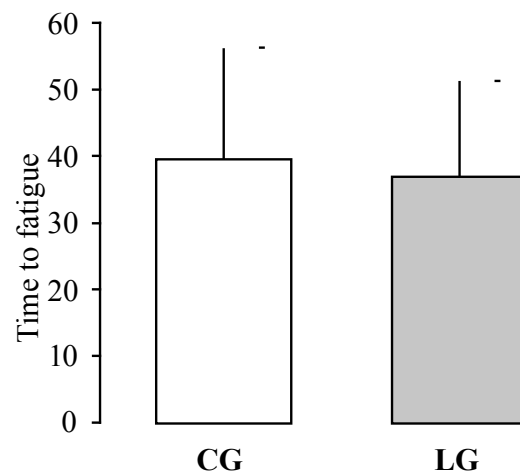
Leprosy patients had a lower MVC compared with healthy subjects ( $p < 0.05$ ), both in the dominant and the non-dominant hand (Figure 2). The time to fatigue in the leprosy and control groups was similar ( $p > 0.05$ ) (Figure 3). As they were free to contract the

muscle without a specific rhythm, we compared the number of contractions completed by each subject. We observed that the leprosy patients had more contractions than the healthy subjects ( $22.6 \pm 11.8$  contractions for the leprosy group vs.  $12.3 \pm 6.9$  contractions for the control group,  $p < 0.05$ ).



Note: A: non-dominant hand; B: dominant hand; CG: control group; LG: leprosy group.

**Figure 2** – Maximum voluntary contraction of the non-dominant and dominant hands.



Note: CG: control group; LG: leprosy group.

**Figure 3** – Time to fatigue.

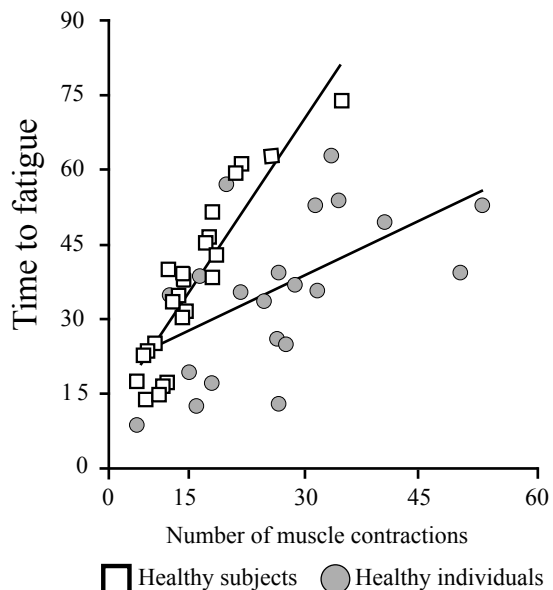


Figure 4 shows the correlation between the number of contractions and the time to fatigue for both groups. We observed that both data were well-fitted with positive linear functions, but with different slopes (control group: high slope; leprosy group: low slope)

**Figure 4** – Correlation between time to fatigue and number of muscle contractions for leprosy and healthy subjects..

## Discussion

The hand grip strength evaluation is an important tool to identify motor function involvement in leprosy. It is an indicator of the general body force [29], and for leprosy patients it can be an activity to inform about muscle force and fatigue.

This investigation showed that leprosy patients had less muscle strength, but similar time to fatigue compared with healthy subjects. Although the time to muscle fatigue is the same for leprosy and healthy groups, we also observed that the leprosy group contracted longer than the control group.

The muscle weakness of the leprosy patients is well known [30-32]. Several investigations have reported leprosy affects the striated muscle [30, 33, 34]. Some authors have suggested muscle tissue has a high affinity to bacteria [30], while others believe the muscle involvement is unrelated to the nerve damage [33, 34]. Muscle involvement in leprosy probably occurs due to these two different mechanisms. The infection occurs through neural, vascular, and lymphatic pathways [35], and the Schwann cells are the bacteria's important target.

*M. leprae* antigen presentation of the Schwann cell elicits an inflammatory response that strikes the infected glial cell. The consequence is that the axon associated with the glia is also damaged by the immune response, resulting in a process of muscle denervation. Another mechanism is the direct muscle involvement with the bacteria. New evidences have suggested *M. leprae* induces Schwann cells to modify for immature migratory cells. The infected immature cells reach other tissues and can be turned into cells of the host tissue, spreading the bacteria in the body [36].

In mice, the muscle denervation led to muscle weight loss, a decrease of muscle force, the development of resting tension, ATP concentration during fatigue, and force recovery after fatigue. These modifications can increase or decrease the resistance of the fatigue in different muscles. The mechanism that underlies these changes is mediated by KATP channels [37].

The effects of bacterial infection in the muscle also support our results of muscle strength loss. *M. leprae* causes loss of striations, changes in sarcolemmal, endomysium thickening, muscle necrosis, and fibrosis [38]. In muscle biopsy specimens from leprosy patients, the main structural change in the muscle tissue was atrophy of its fibers, followed by loss or disorganization of the myofibrillar elements, sarcoplasmic elements, and accumulation of lipofuscin in the lysosome-like bodies. Vascular changes in the intramuscular blood vessels and immune responses should be involved in the structural changes of the muscle fiber [39, 40].

Uniting structural and functional modifications in the muscle tissue, considering that the leprosy causes denervation of muscle fibers, we would expect leprosy patients had muscle strength loss such as in animal models. This study and many reports have shown the decrease of muscle force in leprosy patients. The similarity between the time to fatigue of the patients and control subjects may occur for different reasons. We recruited newly diagnosed and treated patients with few or no clinical sequels caused by leprosy. The hand grip task we evaluated involved many muscle groups that could be differently influenced by the denervation process. The denervation process changes the muscle fiber type from fast contraction fibers to slow contraction fibers [41]. In non-human primates, the muscles involved in the hand grip task, such as the flexor digitorum superficialis muscle and

flexor carpi ulnaris muscle [42, 43], fast contraction muscle fibers prevail. Although no study correlates the type and number of fibers in humans and other primates, this may be an important analogy to understand the difference of fatigue between leprosy patients and healthy subjects. Leprosy denervation has the potential to convert the phenotype of the muscle fibers, thus increasing the resistance to fatigue.

The number of muscle contractions performed by the leprosy patients until the time to fatigue was higher than that of healthy subjects, but this result is difficult to understand. One possibility is that the leprosy patients had less force than the healthy subjects and could stand individual contractions longer. Another reason is that we did not establish any rhythm for the contractions performed during the fatigue test, and the patients may have decided to execute the test at a higher contraction rate than the control subjects.

## Conclusion

Multibacillary leprosy patients showed muscle force loss without a modification on the resistance to fatigue. Muscle involvement and nerve supply should support the results. The protocol of muscle function evaluation could be used to monitor the functional status of the muscles involved in the hand grip test.

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