



Muscle function in women with systemic sclerosis: Association with fatigue and general physical function



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ABSTRACT

Background: Individuals with systemic sclerosis have muscle functions with varying degrees of muscle weakness and atrophy, which in turn can have a negative impact on functional and health-related quality of life. This study aimed to evaluate peripheral muscle performance using isokinetic dynamometry of the knee in women with systemic sclerosis and to correlate peripheral muscle dysfunction with disability levels and general fatigue.

Methods: Twenty-six women with systemic sclerosis and a matched control group with an equal number of women underwent knee isokinetic dynamometry at angular speeds of 75°/s and 240°/s, isometric handgrip strength, the Health Assessment Questionnaire Disability Index, the Functional Assessment of Chronic Illness Therapy-Fatigue scale, and the Fatigue Impact Scale.

Findings: Women with systemic sclerosis showed significant reductions in almost all isokinetic parameters for the two angular velocities tested compared with the controls. An agonist/antagonist ratio with values < 40% was observed in approximately one-third of the patients. These patients had lower isometric handgrip strength. These patients also performed worse on the two general fatigue scales evaluated. Significant correlations were observed between the isokinetic parameters and the measured isometric handgrip strength, and the Health Assessment Questionnaire Disability Index.

Interpretation: Systemic sclerosis patients have reduced strength and endurance as well as a muscle imbalance between the quadriceps and hamstrings. In these patients, lower muscle dysfunction of the knee joint is associated with lower handgrip strength and physical incapacity.

1. Introduction

Systemic sclerosis (SS) is an autoimmune and connective tissue disease characterized by collagen overproduction and deposition, and impairment of the small arteries and capillaries (Chizzolini et al., 2011). Its prevalence is approximately 10 cases per 100,000 population. Over 80% of the cases occur in women (Strollo and Goldin, 2010; Sticherling, 2012). SS can affect various organs and systems, with the skin the most frequently affected site, followed by the musculoskeletal system, lungs, kidneys and heart, which results in a worsening prognosis (Tani et al., 2013).

Skeletal muscle involvement in SS is variable, with a prevalence ranging between 24 and 97% depending on the criteria used to define it, which include clinical, biological, electromyographical and/or pathological findings (Ranque et al., 2007; Morrisroe et al., 2015). SS

patients may have muscle involvement in the form of myositis or non-inflammatory myopathy and present varying degrees of weakness and muscle atrophy (Ranque et al., 2007). Muscle disease in SS was a poor prognosis factor that negatively affected survival, especially in younger patients with early diffuse disease and a high Health Assessment Questionnaire Disability Index (HAQ-DI) score (Jung et al., 2014). One study evaluated 1718 SS patients who had available data on muscle weakness and disability assessed using the Medsger muscle severity score and HAQ-DI, respectively, and found that 22.8% had muscle weakness (Paik et al., 2016). This subset was more likely to experience diffuse cutaneous SS, a shorter disease duration and synovitis than the subset without muscle weakness. With the development of new devices, such as modern isokinetic dynamometers, there is growing interest in more accurately measuring muscle functions in the various conditions that compromise the skeletal muscle.

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Over the past three decades, health status evaluations have undergone a drastic paradigm shift, evolving from a predominant dependence on biochemical measurements to an emphasis on health outcomes based on the patient's own evaluation of his/her disease (Bruce and Fries, 2003). Within this new paradigm, the HAQ-DI has been used as a questionnaire focusing on the skeletal muscles to evaluate the disease's effect on physical function and disability (Sultan et al., 2004). Because of a reduction in muscle mass (affecting muscle strength) is one of the main factors involved in the reduction of mobility and disability in various clinical situations (Kim et al., 2013), HAQ-DI is considered a useful tool for the evaluation in clinical practice (Sultan et al., 2004). However, there are no studies on the association between the HAQ-DI scores and objective measures of peripheral muscle function. In SS, general fatigue negatively affects health-related quality of life (HRQL) and the ability to perform activities of daily living (ADLs) as much or more than any other symptom; the fatigue level in these patients is comparable with the levels reported by cancer patients in active treatment (Thombs et al., 2009). One study showed that 89% of 464 SS patients reported general fatigue at least part of the time, and 72% of these patients indicated that general fatigue had an effect on their ability to perform ADLs (Bassel et al., 2011). Fatigue in SS is still a poorly understood symptom and can be attributed at least in part to muscle function, although several other factors may also be involved in its pathogenesis (Pope, 2003; Strickland et al., 2012). Despite its high frequency, almost 90% of rheumatologists report that they never evaluate fatigue, and few studies have addressed the effect of fatigue on SS patients (Racine et al., 2016; Thombs et al., 2009). Moreover, a possible contribution of muscle dysfunction on the general fatigue of these patients has not been previously evaluated.

Most studies have evaluated muscle disease in SS only in terms of the subjective (Jung et al., 2014; Mimura et al., 2005; Paik et al., 2016; Ranque et al., 2007; Ranque et al., 2009) or isometric (Guillaume-Jugnot et al., 2016; Lima et al., 2015; Schouffoer et al., 2016) measurements. Thus, more accurate and reliable research is needed to demonstrate the real impact of muscle involvement on these patients (Ranque et al., 2009). In this context, isokinetic dynamometry is considered a gold standard for evaluating muscle function. However, to our knowledge, no studies have used this method to assess SS patients. Furthermore, muscle weakness in SS can clearly have a major effect on the functional capacity, which in turn may directly affect the HRQL of these patients. We hypothesize that patients with SS have impaired muscle function, which is associated to general fatigue, physical function and disability. Therefore, the aims of this study were to evaluate peripheral muscle performance in women with SS using knee isokinetic dynamometry and to correlate peripheral muscle dysfunction with the disability and general fatigue levels.

2. Methods

2.1. Subjects

Between October 2015 and July 2016, a matched case-control study was performed to evaluate 33 consecutive women with SS recruited at the Pedro Ernesto University Hospital of the State University of Rio de Janeiro, Rio de Janeiro, Brazil. The inclusion criteria were patients aged over 18 years who met the American College of Rheumatology/European League Against Rheumatism criteria (van den Hoogen et al., 2013) for the diagnosis of SS. The following exclusion criteria were applied: evidence of overlap with other connective tissue diseases except Sjogren's syndrome; major complaint of pain in the knee joint; history of fracture of the lower limbs; presence of neurological deficits; and patients considered "very active" according to the International Physical Activity Questionnaire (IPAQ) (Matsudo et al., 2001). The disease duration was defined as the time from the onset of the first symptom (except Raynaud's phenomenon) to the time of the visit when the patient was included in the study (Racine et al., 2016; Thombs

et al., 2009). A control group of women aged ≥ 18 years was also recruited; the controls were matched by anthropometric variables and physical activity levels and showed no evidence of any musculoskeletal disorder. The protocol was approved by the Research Ethics Committee of the Augusto Motta University Center and complied with the provisions of the Declaration of Helsinki. All subjects signed an informed consent form.

2.2. Measurements

The HAQ-DI was used to evaluate physical disability. This questionnaire evaluates functional capacity levels and includes questions related to the fine movements of the upper extremities, motor activity of the lower limbs, and activities involving both extremities of the upper limbs and the lower limbs with 20 items divided into eight ADL categories (Bruce and Fries, 2003). The HAQ-DI uses a score ranging from 0 (no disability) to 3 (maximum disability) to quantify the values found, with a score of 0–1 representing mild to moderate disability, 1–2 representing moderate to severe disability, and 2–3 representing severe to very severe disability (Bruce and Fries, 2003). To calculate the HAQ-DI value, the maximum scores for each category are added together, and the obtained value is divided by eight to give a score ranging from 0 to 3. A higher score indicates a greater degree of functional impairment. The HAQ-DI has been validated as a measure of disability in SS, and the results of several studies provide evidence of its reliability (Ferraz et al., 1990; Khanna et al., 2005; Poole et al., 1995).

The Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) scale has high internal consistency (Cronbach's alpha > 0.90), good predictive validity and reliability, and is easy to apply (Cella et al., 2005; Parks et al., 2012; Webster et al., 2003). It evaluates the level of tiredness, weakness and difficulty in performing ADLs over the previous week due to fatigue (Cella et al., 2005). The FACIT-F contains 13 items, each of which has a five-point scale (0 = very much to 4 = not at all) in which the sum of all items may vary from 0 to 52. Lower FACIT-F scores indicate greater fatigue (Webster et al., 2003).

The Fatigue Impact Scale (FIS) scale consists of 40 questions related to fatigue over the previous four weeks, which are divided into three domains (cognitive, physical and psychosocial functions). Each question is scored from 0 to 4 from a minimal to a severe degree. The scores range from 0 to 160. In this scale, higher scores indicate greater fatigue. In addition to being a tool that evaluates multidimensional characteristics, the FIS also has the advantage of being easy to use and has good reproducibility (Parks et al., 2012). Its validity and reliability have been demonstrated in a number of studies (Fisk et al., 1994; Lopes et al., 2016a; Pavan et al., 2007).

Isometric handgrip strength (IHGS) was measured using a hydraulic isometric dynamometer (SH5001 Saehan Corporation, Korea) on the hand of the dominant side of the body. The tests followed the recommendations of the American Society of Hand Therapists (Crosby et al., 1994). To standardize the procedure, the participants were seated with the elbow flexed at 90° and the forearm in a neutral position. Three maximal voluntary contractions were performed with an interval of 60 s between tests. This interval produces less fatigue (7%) than 15 and 30 s intervals (10% and 12%, respectively) (Trossman and Li, 1989). The highest value was used for the analysis (Crosby et al., 1994).

The knee joint muscles were evaluated using the Biodex System 4 PRO dynamometer (Biodex Medical Systems, Shirley, NY, USA) from the Admiral Adalberto Nunes Physical Education Center (Brazilian Navy), Rio de Janeiro, Brazil. The test was performed using only the results from the dominant leg. The dynamometer's rotational axis was aligned with the lateral epicondyle of the femur. The range of motion in the test run was measured at 90° starting from 90° with the knee in flexion. Prior to the test, the patient underwent familiarization training with three submaximal repetitions (Felício et al., 2015). After this step, two sets of five repetitions were performed with low (75°/s) and high (270°/s) angular velocities to measure strength and endurance, respec-

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