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Quadriceps strength is a sensitive marker of disease progression in sporadic inclusion body myositis

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Abstract

There are currently no effective treatments to restore the muscle function in sporadic inclusion body myositis. Natural history studies of this disease are scarce. The goal of this study consisted in defining the functional pattern of patients with sporadic inclusion body myositis and to follow its change over a 9-month period to determine the most sensitive outcome measures for future clinical trials. Twenty-two patients with definite sporadic inclusion body myositis were assessed using clinical and functional scales. Dynamometry was used to evaluate the strength for hand grip and wrist, elbow, ankle and knee flexion and extension. Among the patients, 16 were reassessed 9 months later. The mean whole composite index was at $43.3 \pm 16.5\%$ of the predicted normal values. The weakest muscle functions were hand grip, wrist flexion and elbow flexion at the upper limbs and knee extension and ankle flexion at the lower limbs. Muscle weakness was generally asymmetrical, especially for upper limbs where all tested functions were significantly stronger at the dominant side. The patient strength was correlated with the disease duration only for knee extension, which was also the only muscle function to change significantly over 9 months. Knee extension strength seems to be the most relevant marker of disease progression in sporadic inclusion body myositis when measured with suitable dynamometry.

Keywords: Inclusion body myositis; Natural history; Outcome measures; Strength; Dynamometry

1. Introduction

Sporadic inclusion body myositis (sIBM) is the most common acquired inflammatory myopathy in patients over 50 years of age [1]. The physiopathology is unknown but degenerative and auto-immune inflammatory mechanisms are involved [1,2]. To date, there is no validated treatment for this disabling disease. Development of new therapeutic approaches needs sensitive and reproducible evaluation methods to assess their effect on the neuromuscular function. Evaluation of strength in sIBM patients is challenging because of the asymmetric weakness of both proximal and distal upper and lower limb muscles and the slowness of its progression [3]. Natural histories are rather scarce and limited in the number of patients involved. Muscle strength was measured using either handheld dynamometry (HHD) [4] or fixed dynamometry (QMT: Quantified Muscle Testing) [5,6] and was shown to decrease in most patients, but not all.

As new treatments will emerge, robust methods to assess their effects are needed. This study describes the pattern of neuromuscular abilities of patients suffering from sIBM

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using various functional rating scales and dynamometric measures of strength. The aim was to assess the motor function changes within a period of time of 9 months and to determine the most sensitive outcome measures over this period.

2. Materials and methods

2.1. Patients

All patients involved in the study had definite sIBM (i.e. pathological examination of their biopsies showed fibres invaded by lymphocytes, vacuoles and amyloid deposits) [7] and were not treated by any immunosuppressive or immunomodulator drugs for more than 6 months before inclusion. Creatine kinase level at baseline was 434 ± 296 UI/l. The institutional review board approved the study protocol (ClinicalTrials.gov Identifier: NCT00898989); all patients were enrolled after written, informed consent was obtained. Patients were evaluated during two visits 9 months apart.

2.2. Clinical and functional evaluations

During each visit, the same physician performed a conventional clinical muscle strength evaluation by manual muscle testing (MMT using the Medical Research Council (MRC) scale) of 32 muscle groups. Patients were also assessed using two non-specific functional scales (Walton (functional scales evaluating functions of lower limbs) [8] and Rivermead Mobility Index (RMI) [9]) and two specific scales (sIBM weakness composite index (IWCI) [3] and Inclusion Body Myositis Functional Rating Scale (IBMFRS) [10]). The walking ability of the patients was assessed by a six minute walk test.

2.3. Strength assessment

Specific dynamometric measurements were performed to measure hand grip strength and extension and flexion torques for wrist, elbow, ankle and knee. All the tests were performed according to standardized operating procedures (Fig. 1) and were always ordered as follows: grip, wrist, ankle, 6MWT, knee and elbow. Rest periods of 15 s or more if needed were respected.

Isometric hand grip strength was measured using the MyoGrip handle (Fig. 1A) [11]. Its sensitivity is 10 g.

Wrist flexion and extension strength was assessed by measuring the maximal isometric torque generated on a torque meter (Fig. 1B). The device (namely, the MyoWrist) is equipped with a foam cradle and two Velcro straps in order to firmly maintain the forearm within the cradle. Two vertical bars are positioned at the elbow level aiming to avoid lateral movements of the elbow. A U-shaped support is fixed over the torque meter to receive the hand palm within a dense foam cradle. This support is adjustable with respect to the hand length. The MyoWrist sensitivity is 0.01 Nm.

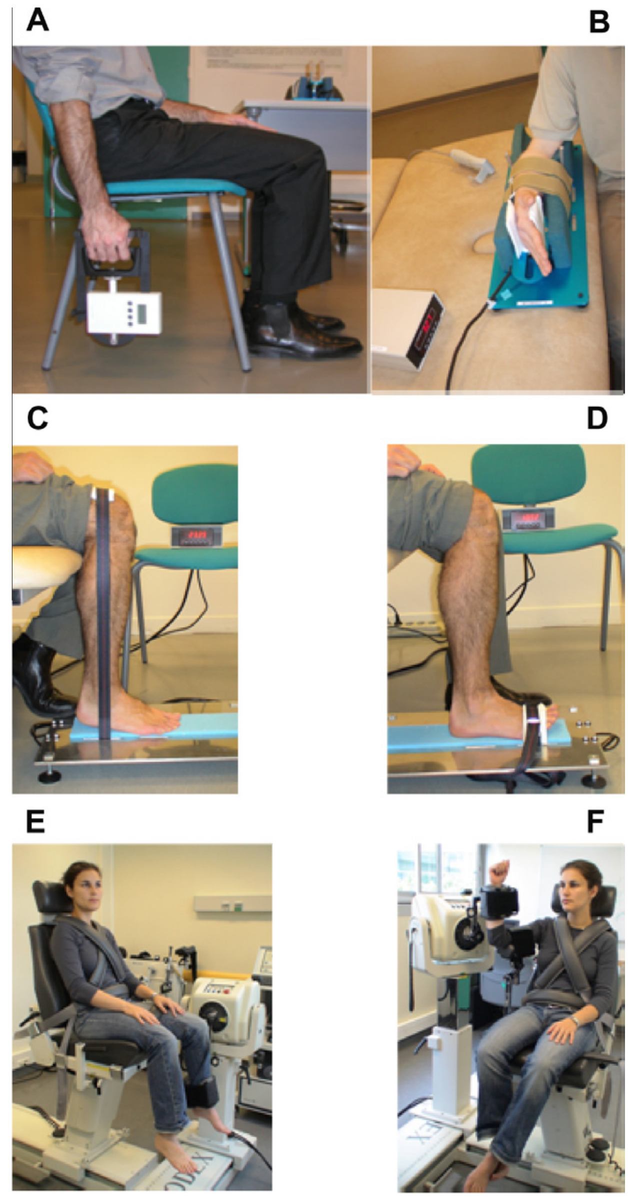

Fig. 1. Strength measurements of several muscle functions by dynamometry. (A) Hand grip. (B) Wrist flexion and extension. (C) Ankle extension. (D) Ankle flexion. (E) Knee flexion and extension. (F) Elbow flexion and extension.

Ankle flexion and extension were measured on a specific device (namely, the MyoAnkle) (respectively, Fig 1C and D). The ankle dynamometer was designed to measure the isometric strength generated around the ankle joint in the extension and flexion directions. It consists in an aluminium plate below which are held two load cells on which strain is applied through an inelastic strap going through slots in the plate. The strap is placed and held either on dorsal part of the foot at the level of the first metatarsian for flexion measurement, or above the knee at the level of epicondyles for extension measurement. To ensure a larger and stiffer support on the knee, the strap was reinforced with a composite material made of two layers of dense