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Original article

Ambulatory capacity in Japanese patients with Duchenne muscular dystrophy

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Abstract

Introduction: Few long-term cohort studies have addressed changes in the ambulatory capacity of patients with Duchenne muscular dystrophy (DMD), and no reports have evaluated the factors associated with ambulatory capacity in Japanese.

Methods: The longitudinal changes in 10-meter run/walk ability and associated factors were retrospectively investigated using general practice data. The factors associated with loss of this ability before the age of 10 years were explored by logistic regression analysis using parameters of genetic mutations, corticosteroid use, the manual muscle test (MMT), and the joint range of motion (ROM). Explanatory variables of MMT grade included hip flexors, knee flexors, and knee extensors; ROM included hip extension, knee extension, and ankle dorsiflexion.

Results: Among 418 patients diagnosed with DMD, 145 patients underwent the 10-meter run/walk test between March 1999 and July 2015. The median age at loss of 10-meter walking ability was 10.4 (interquartile range: 9.2–11.3) years. The 10-meter run/walk speed began to decline 3 years before the loss of 10-meter walking ability, and the median was <1 m/s 1 year before the loss of 10-meter walking ability. MMT grade for knee flexors and ROM for hip and knee extension were identified as independent predictors. Based on the change over time of these three items, limitation of the hip extension ROM preceded knee flexor weakness and limitation of the knee extension ROM.

Conclusions: This knowledge can be used in optimizing rehabilitation programs and evaluating effect of treatment for DMD patients.

Keywords: Duchenne muscular dystrophy; Epidemiology; Natural history; Motor function; Ambulatory capacity; Rehabilitation; Muscle strength; Range of motion

1. Introduction

Duchenne muscular dystrophy (DMD) is a disabling and life-threatening X-linked genetic disorder characterized by loss of dystrophin protein and progressive

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muscle weakness [1]. DMD is the most common neuromuscular disease of childhood and occurs in about 1 in every 3500 male births [2].

According to some reports, patients with DMD lose walking ability with the development of muscle weakness around 10 years after they become able to walk in infancy [3–5]. Few cohort studies describe the long-term natural history of DMD around the world and no reports evaluate the factors associated with ambulatory capacity in Japanese DMD patients. Ambulatory capacity is associated with activities of daily living [6,7]. Rodillo et al. reported that prolongation of walking with orthotic devices prevented rapid progression of scoliosis in DMD patients [8]. In addition, Nätterlund et al. showed that quality of life might depend on physical status, disability, and psychosocial factors in adults with muscular dystrophy [9]. To provide the most appropriate physical care for DMD patients, the progression of disability must be studied in these patients. Therefore, we investigated DMD-related longitudinal changes in ambulatory capacity and identified factors predictive of ambulatory loss using DMD information collected from general practice at a single site.

2. Patients and methods

2.1. Ethical considerations and study design

This study was conducted in accordance with the ethical guidelines for epidemiological research (issued by the Ministry of Education, Culture, Sports, Science and Technology and the Ministry of Health, Labour and Welfare on December 1, 2008). Prior to the start of this study, protocol approval was obtained from the Ethics Committee of Kobe University Graduate School of Medicine. The study design was retrospective- and cohort-based, and the DMD data were obtained from general practice in Kobe University Hospital.

2.2. Patients

As the data source, we used the dystrophinopathy database in the Department of Pediatrics, Graduate School of Medicine, Kobe University, which includes clinical data since 1999. DMD patients who underwent a 10-meter run/walk test before July 2015 were included in this study. DMD was diagnosed based on genetic testing or muscle pathology and patients with other types of muscular dystrophy were excluded. Gene mutations were analyzed using not only genomic DNA, but also mRNA extracted from muscle as described before [10].

2.3. Assessments

The ability or inability to run or walk 10 m was assessed in patients aged 20 years or younger and as a function of age. In the 10-meter run/walk test, DMD patients were instructed to run or walk as fast as possible from a starting line to a point 1–2 m ahead of a goal line, where a physical therapist (PT) was standing. One measurement of ability to walk 10 m was made per test. In DMD patients not undergoing the 10-meter run/walk test at all pre-specified ages, the test result was recorded as "able" if the patient was "able" to walk in previous and subsequent tests; "unable" if the patient was unable to walk in previous and subsequent tests; "no data (last time was able)" if the patient was able to walk in the previous test but "unable" to walk in the subsequent test; "no data (last time was unable)" if the patient was "unable" to walk in the previous test and "able" to walk in the subsequent test or the test was not performed. Even if the result changed from "able" to "unable," patients with long measurement intervals were excluded from the identification of the age at loss of 10-meter walking ability. The measurement interval was defined as long if the age at last "able" result was 2 or more years younger than the age at first "unable." The 10-meter run/walk speed data were tallied over the 5-year interval prior to the 10-meter run/walk test for patients in whom the age at loss of 10-meter walking ability could be identified. The manual muscle test (MMT) grades and joint range of motion (ROM) were measured bilaterally in accordance with published methods [11–13]. The 10-meter run/walk test, MMT, and ROM were measured by a well-trained PT and occupational therapist (OT) pair. When compensatory action occurred during MMT, the evaluator or another staff member held the patient and recorded the results excluding the compensatory action. Two PTs were involved in the study, because the acting PT had changed during the study period. There was no change of OT during the study, and therefore only one OT was involved. The patients underwent rehabilitation usually once every 3–6 months.

2.4. Predictors and data analysis

The factors associated with mobility loss (inability to walk 10 m) before the age of 10 years in DMD patients were analyzed by forward stepwise logistic regression with the following explanatory variables: genetic mutations (exonic deletion, exonic duplication, others), corticosteroid use, MMT parameters related to the lower part of the body (of the parameters measured in general practice, such as the strength of neck flexors, shoulder abductors, elbow flexors, elbow extensors; here, the hip flexors, knee flexors, and knee extensors) and ROM parameters (hip extension, knee extension, and ankle dorsiflexion), which were measured for the first time at the age of 10 years. For measurements that could not be made at the age of 10 years, the values obtained at the time closest to the 10th birthday (allowance: age 8–12 years) were used. When investigating the relationship

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