Hindawi
Acta Neurologica Scandinavica
Volume 2023, Article ID 8373917, 9 pages
https://doi.org/10.1155/2023/8373917

Review Article

Instruments and Parameters for Evaluating Upper Limb Motor Fatigability in Individuals with Neuromuscular Diseases: Systematic Review

Danila Cristina Petian-Alonso,[1] **Camila Scarpino Barboza Franco**,[1] **Emanuela Juvenal Martins**,[1] **Karoliny Lisandra Teixeira Cruz**,[1] **Roberta de Fátima Carreira Moreira Padovez**,[2] **and Ana Claudia Mattiello-Sverzut**[1]

[1]*Department of Health Sciences, Ribeirão Preto Medical School, University of São Paulo, Brazil*
[2]*Núcleo de Avaliação de Tecnologias em Saúde, Hospital Sírio-Libanês (NATS-HSL), Brazil*

Correspondence should be addressed to Ana Claudia Mattiello-Sverzut; acms@fmrp.usp.br

Received 12 September 2022; Revised 3 June 2023; Accepted 8 September 2023; Published 13 October 2023

Academic Editor: Luigi Trojano

Background. Neuromuscular diseases present a set of clinical and pathological disabilities that include muscle weakness and atrophy, perception of fatigue, fatigability, and contracture. Motor fatigability compromises the ability of the individual to generate muscle strength and perform their daily activities. Quantitative measures of strength and motor fatigability are important to determine the clinical progression of the disease and the response to the proposed treatments. Thus, the aim of this study was to identify the equipment and protocols frequently used to assess upper limb motor fatigability in patients with neuromuscular disease. *Methods*. Information such as equipment used to induce motor fatigability, body segment or joint studied, movement analyzed, type of contraction, and protocol utilized for the test was analyzed. Joanna Briggs Scale and Newcastle-Ottawa Scale assessed the methodological quality of the studies. In addition, a checklist was prepared by the research group to assess the protocols presented in the referred studies. *Results*. The isokinetic and handgrip dynamometers were the most utilized equipment to induce motor fatigability. 83% of the studies had a design with low methodological rigor and half of them with high risk of bias. In the analysis of the protocols utilized to induce motor fatigability, one study was classified as regular and the other ones as good. *Conclusion*. The methodological topics to assess motor fatigability were incompletely described considering the electrophysiological and biomechanical approach. Although the motor fatigability in the upper limb was evaluated using isokinetic and handgrip equipment, the absence of a gold standard protocol still compromises the understanding of clinical progression and responses to the treatments in the neuromuscular diseases. This trial is registered with CRD42021206934.

1. Introduction

Fatigue is a common symptom of many chronic diseases, but the lack of standardized definitions and measurement has made it difficult to assess this condition accurately. The term fatigue has been the subject of discussions that seek unification regarding the use of this terminology. Kluger et al. [1] proposed a taxonomy that divides the term fatigue in two domains: perception of fatigue and fatigability. In this model, perception of fatigue refers to subjective sensations of weariness, which can be measured using self-report scales capable of assessing the individual's perception of fatigue. In turn, the term fatigability refers to objective changes in one or more aspects of the individual's performance when performing a prolonged task or when comparing performance before and after performing a fatigue-inducing task. Furthermore, this taxonomy proposes that fatigability be understood under the cognitive and motor domains. In the motor domain, fatigability is quantified by the decline in peak strength, power, and speed when performing the proposed task, whether prolonged or fatigue-inducing. In this study, we adopted the term fatigability in its motor domain.

Neuromuscular diseases enclose a group of disorders affecting the peripheral nervous system, including motor neurons and sensory neurons, muscle, or neuromuscular junction [2]. This heterogeneous genetic or acquired group of diseases manifests with onset from birth to adulthood and with slow or rapid progression [2]. A mix of clinical and pathological disabilities often causes proximal or distal muscle weakness and atrophy, perception of fatigue, fatigability, contractures, stiffness, cramps, or sensorial signs and symptoms [2–4]. Muscle atrophy is one of the hallmark signs of NMD, and it is associated with impairment of muscle strength and the ability to perform daily life activities [5]. Motor fatigability is another challenge for patients with NMD because it involves the loss of force generation during a task or the ability to generate maximal force during repeated or sustained muscle contraction [6].

Quantitative measures of strength and motor fatigability are essential in determining clinical progression and assessing responses to the treatment. The isokinetic dynamometer is a method widely used in laboratory settings. It allows for objective muscle testing using dynamic or static muscle contraction, the force produced during the test uses constant velocity and resistance accommodation, and it can both quantify several characteristics of muscle conditions (such as peak torque, work, fatigue index, and time to reach peak torque) and monitor minor changes in muscle condition [7].

In addition, it is often difficult to extrapolate data from one human motor fatigability study to another since a wide range of concepts, protocols, and methods have been applied by investigators over several decades. The studies must provide specific information about the tools and procedures to investigate motor fatigability.

The natural progression of NMD leads to increasing weakness and musculoskeletal deformities, ambulation loss can happen, and the impairment of the upper limbs can lead to a significant level of activity limitations and restriction in participation [8]. Lower limb muscle groups, especially knee extensors, have been selected to evaluate the motor fatigability process [9] because of their greater muscle mass and volume and their mobility and locomotion functions. On the opposite, upper limbs were rarely explored [10, 11].

In this context, three relevant facts must be recognized for the assessment of motor fatigability in patients with NMD: (1) methodological heterogeneity, (2) fewer studies applied isokinetic dynamometer in patients with NMD, and (3) upper limbs are undersized in both NMD patient assessments and motor fatigability protocols. Thus, this study is aimed at identifying the equipment and protocols frequently used to assess upper limb motor fatigability in patients with neuromuscular diseases. This article will analyze the methodological quality of published articles, presenting evidence that the upper limb of patients with NMD and motor fatigability protocols deserve more consistent scientific investigations.

2. Methods

2.1. Registration Protocol. This systematic review was registered in the International Prospective Register of Systematic Reviews-PROSPERO-ID CRD42021206934.

2.2. Eligibility Criteria. This systematic review included studies that (a) used equipment or functional activities to evaluate upper limb motor fatigability; (b) evaluated the upper limbs and the upper limb joints, or compared the upper limb with the lower limb; (c) used protocols with maximal and/or submaximal voluntary contractions, and (d) were published over the past ten years, as in this period publications related to the subject studied appear more consistently in the literature, and e) in Portuguese and English.

Studies designed as case reports, meeting reports, reviews, and systematic reviews, as well as studies exclusively assessing perception of fatigue (mental, psychological) and motor fatigability resulting from electric stimulation, were all excluded.

2.3. Sources of Information. The research was conducted based on the databases PubMed, Embase, Literatura Latino-Americana e do Caribe em Ciências da Saúde (LILACS), Biblioteca Virtual de Saúde/Biblioteca Regional de Medicina (BVS/BIREME), Cumulative Index to Nursing and Allied Health (CINAHL), Scientific Electronic Library Online (SciELO), and MEDLINE Complete, of EBSCO, between August and October 2020.

2.4. Search Strategy. The research question and the search string were defined using the PICO (patient, intervention, comparison, and outcomes) as a reference [12]. Therefore, the describers were grouped into four blocks: the first is related to the population included in the study (neuromuscular disorder, neuromuscular disease, and neuromuscular); the second is related to the body segment evaluated in the study (upper limb, arm, upper extremity, shoulder, elbow, wrist, and hand); the third block included describers referring to the intervention (isokinetic, evaluation, assessment, torque, dynamometry, and dynamometer); and the fourth block included the outcome (fatigue, muscle fatigue, motor fatigability, and muscle endurance). The Boolean operators "OR" and "AND" were used within and between the blocks, respectively. Quotation marks (" ") were used in terms formed by two words, such as "upper limb."

In this way, we used the string ("neuromuscular disorder" OR "neuromuscular disease" OR neuromuscular) AND ("upper limb" OR arm OR "upper extremity" OR shoulder OR elbow OR wrist OR hand) AND (isokinetic OR evaluation OR assessment OR torque OR dynamometry OR dynamometer) AND (fatigue OR "muscle fatigue" OR "motor fatigability" OR "muscle endurance").

Two independent researchers conducted the entire process. The articles from the research databases were imported to the EndNote reference manager (EndNote Clarivate Analytics®, online version).

2.5. Study Selection. The studies resulting from the search process were submitted to a filter, available in the EndNote reference manager, which excluded duplicate articles. The articles were selected by two independent researchers, and the outcome was discussed until a common understanding was reached by them. We selected the studies by reading the titles and abstracts, and those that did not agree with the review objective were excluded. The remaining article

studies were fully read. If a common understanding could not be reached, a third researcher would be consulted.

2.6. Data Extraction. A protocol was developed for data extraction from each study included in this review. Initially, the general data from each study were extracted, such as author, year of publication, title, objectives, study design, population studied, age, and type of locomotion. Data regarding the protocol to generate motor fatigability was subsequently collected, with a focus on the functional task or equipment, body segment or joint, movements evaluated, type of contraction or exercise, number of repetitions or contractions, time of contraction, preparation for the test, and test details. Variables analyzed included strength, peak torque, work, power, root mean square (RMS), electromyographic signal amplitude, median frequency, mean frequency, and linear envelope. Data on data processing and statistical analysis of the selected studies were also collected.

When the authors reported a decrease in strength/torque or a decline in physical performance, we confirmed it as motor fatigability, regardless of its magnitude.

2.7. Risk of Bias. Studies selected in this systematic review were designed as nonrandomized (cohort, cross-sectional, and case-control designs). Therefore, we used the Newcastle-Ottawa Scale (NOS) to assess the methodological quality of the cohort and case-control studies and the Joanna Briggs Scale (JBS) for evaluating the cross-sectional studies.

The NOS was developed to assess the methodological quality of nonrandomized studies [13]. It is an easy-to-understand and easy-to-apply scale that uses the star system to assess the selected studies [14]. It is divided into three domains that indicate a maximal number of possible stars in each one of them, adding up to a maximal total of nine stars for each study assessed: (1) study group selection (four stars), (2) comparability between study groups (two stars), and (3) exposition assessment (three stars), or (3) outcome of interest (three stars) for case-control or cohort studies, respectively [13–15]. If the study obtains ≥ 7 stars, it means a low risk of bias, and if it is <7 stars, it means a high risk of bias.

JBS assesses the methodological quality of selected articles in a systematic review. The method used to assess cross-sectional studies includes nine questions that can be answered with yes, no, not clear, and not applicable [16]. If the study has less than five items, it means a high risk of bias.

2.8. Assessment of the Motor Fatigability Protocol. In order to check if the studies included in this review used feasible and effective protocols to induce motor fatigability, we prepared a checklist containing eight questions based on its concept, i.e., the decline of muscle performance during or after a motor task.

The answers were presented in the form of a Likert-type scale with four levels (no, partially, yes, and not applicable). A score was attributed to each answer (no, zero points; partially, one point; yes, two points; and not applicable, no score). A total was calculated based on the sum of points, and then, the quality of the article was classified as good (10-16 points), regular (9-5 points), and bad (0-4 points).

3. Results

3.1. Study Selection. The initial research resulted in 653 articles. Among them, 125 were duplicated and excluded. Of the 528 remaining studies, 522 were excluded considering the eligibility criteria. Thus, after reading the title, abstract, and full text, 6 studies were included in this review (see Figure 1).

3.2. Characteristics of the Studies. In total, one hundred and twelve patients with neuromuscular diseases participated in the studies included in this review, of which seventy-three had a clinical diagnosis of myasthenia gravis [17–19], twenty-six patients had a clinical diagnosis of myotonic dystrophy [20], eight had Charcot-Marie-Tooth disease [21], and five had dystrophinopathy [22]. They were aged between 9 and 80 years, and 52.6% were male (see Table 1).

Two studies used an isokinetic dynamometer (Biodex Multi-Joint System®) [17, 18], one study used a force transducer (Kistler, model 9203) associated with electromyography (BTS pocket) [21], one study used a hydraulic hand dynamometer (Rehaforum Medical) [19], and one study used a handgrip dynamometer (Multi-Myometer) [20]. These studies induced motor fatigability through maximal [17, 18] and submaximal [19–21] isometric contractions. Two other studies used upper limb functional tasks [19, 22] to induce and evaluate motor fatigability with dynamic contractions (see Table 2).

3.3. Quality of the Studies Included. Two scales were used to assess the methodological quality of the studies included in this review: NOS and JBS. Of the six studies included, one study [18] was assessed using NOS by its form for cohort studies and scored nine stars and was classified as low risk of bias. Four studies [17, 19, 21, 22] were assessed using NOS by a form for case-control studies, with two studies [17, 19] receiving seven stars, classified as low risk of bias, and two studies [21, 22] receiving a score lower than seven stars, classified as high risk of bias. One study with a cross-sectional design [20] was assessed by JBS, had three compliant items of the eight available, and was classified as high risk of bias (see Table 1). This analysis showed a high risk of bias for 50% of the studies [20–22], indicating as main problems the absence of (a) the origin of the control group [22], (b) information about the patient loss throughout the study [21, 22], and (c) details in the description of the statistical analysis and inclusion criteria [20].

Considering the analysis of the test protocol by the checklist, these studies presented partial descriptions or absence of description of items considered important for the protocol, such as (a) warming-up [17–19, 21, 22], (b) familiarization [19–22], (c) positioning [19, 22], (d) ROM evaluated [18, 19, 22], (e) rest interval [19, 22], (f) description of data processing and analysis [18, 20], and (g) absence of the number of volunteers who did not complete the protocol [21, 22]. However, only one study [22] was classified as regular for not presenting information on muscle warm-up,

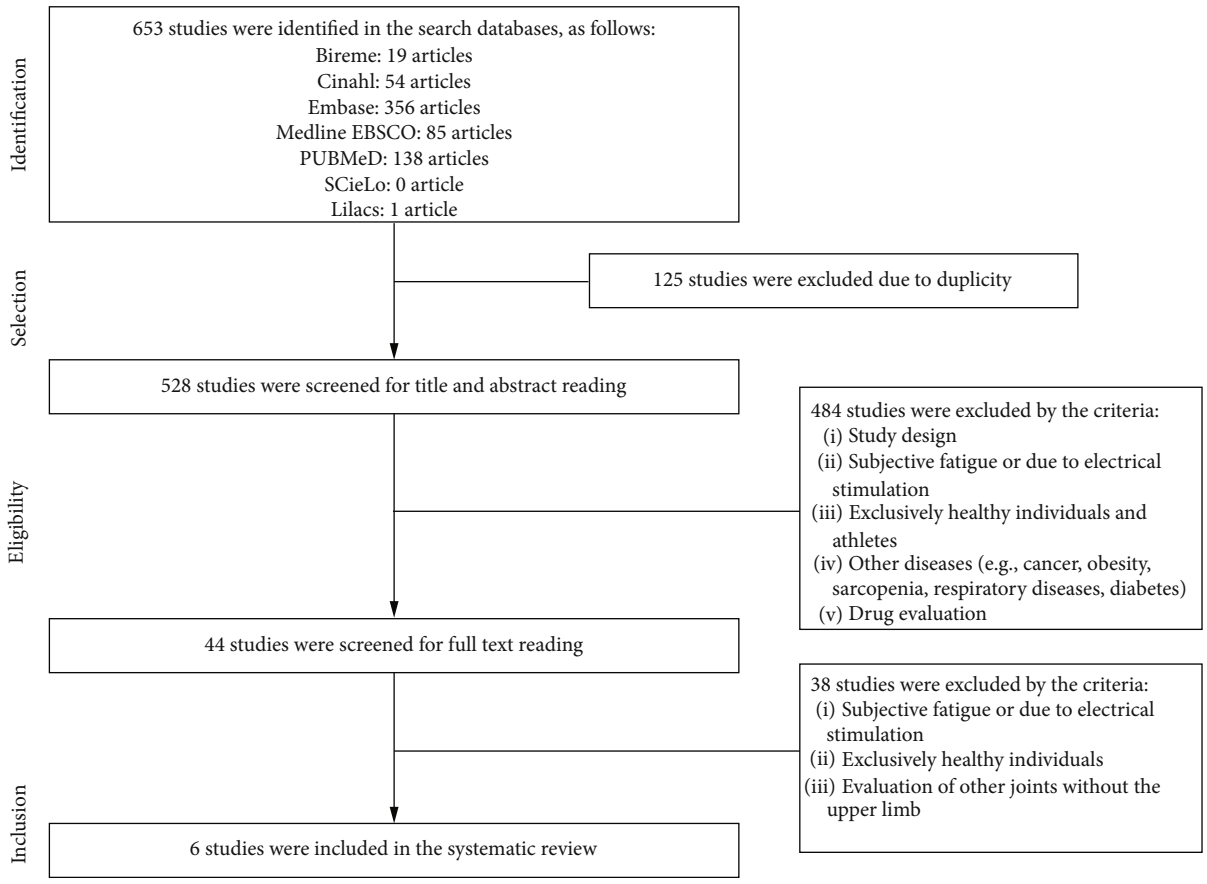

Figure 1: Flowchart of the literature search.

Table 1: Study characteristics.

Authors	Study design	RB	Diagnosis	Included patients		Included healthy	
				N	Mean age (y) (SD)	*N*	Mean age (y) (SD)
Symonette et al. [17]	Case-control	Low	MG	ND-MG: 8 (6 men) D-MG: 12 (6 men)	ND-MG: 54.3 (16.8) D-MG: 52.8 (17.2)	21	53.8 (20.3)
Menotti et al. [21]	Case-control	High	CMT1A	8 (3 men)	35.9 (9.9)	8 (3 men)	35.1 (11.2)
Lowes et al. [22]	Case-control	High	D	5 men	Range 9-36*	5 men	-
Vinge and Andersen [18]	Cohort	Low	MG	21 (13 men)	Range 19-80*		
Jordan et al. [19]	Case-control	Low	MG	32 (9 men)	55.7 (3.1)	17 (5 men)	46.5 (17.9)
Baldanzi et al. [20]	Cross-sectional	High	MD	26 (17 men)	41.6 (12.7)		

Legend: a hyphen (-) indicates not specified. * indicates that the authors did not present mean age. Abbreviations: *N*: number of participants; RB: risk of bias; MG: myasthenia gravis; CMT1A: Charcot-Marie-Tooth type 1A; D: dystrophinopathy; MD: myotonic dystrophy; D-MG: decrement on repetitive nerve stimulation MG; ND-MG: not decrement on repetitive nerve stimulation MG.

the familiarization of the patient with the equipment, positioning, range of motion (ROM) evaluated, rest interval, and the number of volunteers who did not complete the protocol. All other studies were classified as good (see Table 3).

4. Discussion

This systematic review summarizes the equipment and measurement protocols that assessed upper limb motor fatigability in patients with neuromuscular diseases. Furthermore, it analyzed the effectiveness of each protocol in inducing motor fatigability.

The terms fatigue and fatigability deserve caution to be an assumption in scientific studies. Fatigue is a clear term knowledge to all, but several synonyms, or related terms, can be found in the literature such as peripheral and central, muscular and mental, motor and cognitive, and physiological and pathological. Kluger et al. [1] proposed a taxonomy

Table 2: Motor fatigability protocol description.

Authors	Instrument	Segment/ joint/muscle	Movement	Type of contraction	Contraction intensity	Series	Repetitions	Contraction/ rest time
Symonette et al. [17]	Isokinetic dynamometer[a]	Shoulder	Abduction	Isometric	Maximal	1	12	4 sec./1 sec.
Vinge and Andersen [18]							13	5 sec/5 sec.
Menotti et al. [21]	Force transducer[b]+EMG[c]	Elbow[a] Biceps brachii[b]	Flexion	Isometric	Submaximal	1	1	Decrease in target MVC
Baldanzi et al. [20]	Handgrip dynamometer[d]	Hand	Handgrip	Isometric	Submaximal	1	3	60 sec./60 sec.
Jordan et al. [19]	Hydraulic hand dynamometer[e]	Hand	Handgrip	Isometric	Submaximal	1	1	Decrease in target MVC
Lowes et al. [22]	AMT	Upper limb	-	Dynamic	NA	6	All possible	15 sec.
	Motion analysis system	Upper limb	Reach	Dynamic	NA	1	3 of game 2	-
	Software ACTIVE	Upper limb	Reach	Dynamic	NA	1	3 of game 1/3 of game 2	-

Legend: Manufacturer: [a]Biodex Multi-Joint System 3; [b]Kistler, model 9203; [c]BTS pocket; [d]Multi-Myometer; [e]Rehaforum medical. Note. A hyphen (-) indicates not specified. Abbreviations: NA: not applicable; EMG: electromyography; MVC: maximal voluntary contraction.

Table 3: Motor fatigability protocol assessment checklist.

Author/year			1	2	3	4	5	6
Motor fatigability test protocol	Was the segment warmed?		N	N	N	N	N	Y
	Was the familiarization with the equipment done?		Y	N	N	Y	N	N
	Was it described in the protocol?	The position of the volunteer	Y	Y	N	Y	N	Y
		The muscles/movements tested	Y	Y	Y	Y	Y	Y
		The preparation and the placement of electrodes when EMG was used	NA	Y	NA	NA	NA	NA
		The ROM assessed	Y	Y	N	N	N	Y
		The type of contraction	Y	Y	Y	Y	S	Y
		The parameter to be reached in the motor fatigability protocol	Y	Y	Y	Y	S	Y
		The rest break	Y	Y	N	Y	N	Y
	Was verbal or/and visual encouragement used?		Y	Y	Y	Y	PA	Y
	Was the description of outcome variables shown?		Y	Y	Y	Y	Y	Y
	Was the processing description and data analysis presented?		Y	Y	Y	PA	Y	PA
Motor fatigability test results	Was the decline in force/torque or functional task performance or modifications in EMG variables (increase in RMS signal amplitude and/or decrease in median/mean frequency) declared?		Y	Y	Y	Y	Y	Y
	Was the number of volunteers who did not complete the motor fatigability protocol indicated?		Y	N	N	Y	Y	Y
Total score*			14	10	9	13	10	13

Legend: 1: Symonette et al.[17]; 2: Menotti et al.[21]: 3: Lowes et al.[22]; 4: Vinge and Andersen[18]: 5: Jordan et al.[19]: 6: Baldanzi et al.[20]. Abbreviation. Y: yes; N: no; NA: not applicable; PA: partial. *10-16 points: good; 5-9 points: regular; 4-0 points: bad.

for fatigue distinguishing perception of fatigue and objective decrement of motor and or cognitive performance (fatigability). Adopting the terminology proposed by previous authors enables the standardization of scientific studies and favors the rationality required to develop therapeutic strategies for specific diseases.

4.1. Methodological Quality. The design of the selected studies is quite heterogeneous, which targeted the methodological quality assessment to two instruments: JBS in its form to assess cross-sectional studies [20] and NOS in its forms for cohort [18] and case-control [17, 19, 21, 22] studies. The low methodological rigor found in these studies increases the risk of bias, undermining the reproducibility and compromising the results presented by the studies.

4.2. Equipment. The isokinetic dynamometer is described as a gold standard instrument for motor fatigability analysis. This equipment allows for accurate assessment of motor fatigability using isometric or dynamic voluntary contractions. El Mhandi and Bethoux [23] identified that the isokinetic test is appropriate and safe for assessing patients with neuromuscular diseases. The above authors described their difficulty in stabilizing the patient during the test and identified a lack of standardized protocols for the assessment of isokinetic strength [23].

The analysis of the electromyographic signal through surface EMG is useful in studying motor fatigability [24]. In an isometric contraction, there is a reduction in the conduction signal in the sarcolemma and, therefore, a reduction in the median frequency [25]. Furthermore, there is a simultaneous increase in the recruitment of muscle fibers and the amplitude of the electromyographic signal [25]. Therefore, motor fatigability can be marked with increased amplitude and (or) decreased frequency of the electromyographic signal.

In this way, it is possible to detect the level of motor fatigability by analyzing the frequencies and components of the power spectrum [26]. However, it is important to emphasize that electrical activity in the muscle is evaluated, but it is not possible to directly verify the recruitment of motor units [27]. In this review, only one study used EMG to evaluate motor fatigability [21].

The dynamometer isokinetic and surface electromyography are valuable tools to assess patients with neuromuscular diseases and analyze the progression of the rehabilitation process. However, some limitations in using both equipment are their higher cost, the operator being a trained professional, and the higher time expended to perform a full test.

The handgrip dynamometer is a portable and low-cost device with high reliability and allows for obtaining strength values quickly and safely [28]. It has been widely used to assess motor fatigability in neuromuscular [19, 20, 29, 30] and neurological [31–35] diseases. Therefore, the handgrip dynamometer could be an alternative tool to evaluate upper limb motor fatigability since it has reproducibility and reliability properties.

Functional dynamic activities are also described as instruments for assessing motor fatigability [36]. In this modality, the ability of the individual to perform a motor task or movement is assessed using specific parameters, such as intensity, time, and/or number of repetitions until exhaustion [23]. In this review, two studies used functional tasks to induce motor fatigability: the Arm Movement Test (AMT) [19] and the ACTIVE Software [22].

In the AMT, the patient was instructed to hold a 500 g weight with the arm extended horizontally and move it repeatedly between two points, drawing 1/4 of a circle horizontally for 90 seconds [19]. The authors quantified motor fatigability as a decline in proximal muscle performance during repeated movements. Therefore, they believe that this tool can be useful for patients in advanced stages of myasthenia gravis who do not respond satisfactorily to routine clinical tests.

The ACTIVE Software is a tool developed to measure the volume, velocity, and rate of motor fatigability in the functional range of the upper limb in dystrophinopathy [22]. It uses Microsoft Kinect for Windows as an interface that captures the movement while the person performs two ACTIVE games. In this pilot study, the authors aimed to assess the feasibility of the software [22].

Few studies use functional tasks to assess motor fatigability due to the difficulty in quantifying it. This review identified two studies that used functional tasks to assess motor fatigability [21, 22].

4.3. Protocols. Through the checklist application, we searched the protocols for information on the following factors: warm-up of the segment, familiarization with the equipment, positioning and stabilization of the patient, rest between sets, and encouragement (verbal and visual) [37].

Muscle warm-up prior to the motor fatigability test has been described in the literature to prevent injuries [38]. In isokinetic tests, it is recommended that warm-up is done through submaximal efforts with three to eight repetitions, followed by one to three maximal efforts [39]. Among the studies that used the isokinetic equipment [17–19], none used warm-up as a previous step to perform the motor fatigability test. Baldanzi et al. [20] used the Multi-Myometer® equipment and described performing 4 or 5 series of intermittent hand contractions to warm up the segment to be tested. The other studies did not present a description of warm-up before the test [19–22].

Familiarization with the equipment is essential for understanding the movement and direction [38] and was mentioned in two studies used here [17, 18]. The longer or shorter time expended in familiarization is dependent on the size of the muscle groups involved in the movement that induces motor fatigability [40].

Two studies [19, 22] did not present information on the positioning of the patient to perform the test, and three studies [18, 19, 22] did not inform the joint position and ROM. According to De Ste Croix et al. [38], the patient positioning and stabilization adopted in the protocol can influence torque production.

Rest time between repetitions (or contraction series) should be determined according to (a) the population studied, (b) articulation evaluated, and (c) speed performed. For

knee flexion and extension, the rest time can vary from 30 seconds to 5 minutes [41, 42]. Perrin [43] believes that, for the adult population, 30-60 seconds is considered satisfactory rest time for recovery after four repetitions of maximal voluntary contraction. Two of the studies included did not present information about the rest time between repetitions and sets in the motor fatigability test [19, 22].

Motivational factors positively impact the ability of a patient to reach their performance during a physical test. Baltzopoulos and Kellis [44] suggested that verbal and visual feedback improve the children performance to produce force. Belkhiria et al. [45] studied the influence of verbal encouragement on the production of maximal voluntary strength and the rate of maximal strength development using a grip dynamometer and EMG. According to the authors, verbal encouragement significantly increased force production, and the surface electromyography was sensitive to that modification [45]. All studies in this review presented verbal and (or) visual encouragement as a resource for the patient to achieve maximal performance.

The evaluation of data processing and analysis is important because motor fatigability can be calculated: (a) based on the change, in percentage, in peak force, torque, or work after a set time, for example, 10 seconds; (b) after a certain number of repeated submaximal contractions, such as 40 consecutive knee flexion-extension movements; and (c) through a time parameter, determining the ability to perform muscle activity at a defined intensity, until exhaustion [23]. In addition, presentation of the analysis and data processing favors the reproducibility of the study. Only two studies included in this review did not present information related to data processing obtained in dynamometric tests using both the isokinetic [18] and the handgrip [20] devices.

Another important aspect is the declaration of the sample size that could not complete the protocol, also called the nonresponse rate. Patients with neuromuscular diseases have different degrees of muscle weakness, evidencing impairment of the various subsystems involved in muscle contraction, compromising participation of some patients in the test. Thus, we believe that this information can help understand the influence of factors such as age, sex, time of diagnosis or stage of the disease, level of physical activity on motor fatigability, and the disease itself. In addition, it may indicate whether these protocols can be applied at any stage of neuromuscular diseases. In the analysis performed by the checklist and the NOS, two studies [21, 22] did not present information on the nonresponse rate.

We noted that only one study was classified as regular [22] after applying the checklist. The authors of the mentioned article did not present in the test protocol information about warming-up, familiarization, positioning, ROM evaluated, rest interval, and the volunteers who dropped out throughout the study. The methodological quality of the same study was classified as high risk of bias using the NOS. The other studies had both, their test protocol, and the capability to produce motor fatigability, which was classified as good using the checklist.

There is no description in the literature of a gold standard protocol for assessing upper limb motor fatigability in patients with neuromuscular diseases. The selected studies are heterogeneous in design, test conditions, muscles or movements tested, positioning and stabilization of the patient in the equipment, type of muscle contraction evaluated, rest period between attempts, analysis and data processing, and verbal and/or visual encouragement. Therefore, we found studies with low methodological quality, a high risk of bias, and lack of relevant details in the motor fatigability test protocols.

4.4. Study Limitations. This systematic review evidenced the absence of studies available in the literature on the topic addressed. Furthermore, the comprehensive scope of this review showed heterogeneity in the populations approached, motor fatigability assessment methods, and outcome measures that precluded a quantitative analysis (meta-analysis) of the data. In addition, we did not critically assess each study for their internal and external validity. This analysis may be explored in future research. In addition, studies that evaluated changes in fatigue after drug therapy or motor fatigability after an exercise program, and studies that used electrical stimulation, were not included in this review.

5. Conclusion

This systematic review identified that isokinetic and handgrip dynamometers are the most used equipment for assessing upper limb motor fatigability in patients with neuromuscular diseases. Although there is no description of a gold standard protocol, most studies presented in this review have the relevant topics for the motor fatigability assessment described incompletely. Since neuromuscular diseases present a decline in muscle strength as stages of the disease progression, it is important to carry out studies that seek the standardization of protocols that assess motor fatigability. However, this review showed that motor fatigability in these individuals needs to be investigated based on the proposition of studies that establish greater methodological rigor, with the inclusion of evidenced variables and analysis, as well as standardized test protocols to guarantee the reproducibility of the studies.

Data Availability

Data will be available on request.

Conflicts of Interest

The authors declare that there is no conflict of interest regarding the publication of this paper.

Acknowledgments

We thank Cyntia Rogean de Jesus Alves de Baptista and Gabriela Barroso de Queiroz Davoli for contributing to the research's conception. This work was supported by the Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP) (grant 17596-4/2017). DCPA, CSBF, KLTC, and EJM received support through a scholarship from the Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES), Brazil (process 88887.887517/2023-00, process

88887.684910/2022-00, process 88887.817059/2023-00, and process 88887.817066/2023-00, respectively).

References

[1] B. M. Kluger, L. B. Krupp, and R. M. Enoka, "Fatigue and fatigability in neurologic illnesses: proposal for a unified taxonomy," *Neurology*, vol. 80, no. 4, pp. 409–416, 2013.

[2] B. M. Morrison, "Neuromuscular diseases," *Seminars in Neurology*, vol. 36, no. 5, pp. 409–418, 2016.

[3] R. J. Barohn, M. M. Dimachkie, and C. E. Jackson, "A pattern recognition approach to patients with a suspected myopathy," *Neurologic Clinics*, vol. 32, no. 3, pp. 569–593, 2014.

[4] H. L. Fossmo, E. Holtebekk, K. Giltvedt, A. R. Dybesland, P. S. Sanaker, and K. Ørstavik, "Physical exercise in adults with hereditary neuromuscular disease," *Tidsskr Nor Laegeforen*, vol. 138, no. 11, 2018.

[5] C. M. McDonald, "Physical activity, health impairments, and disability in neuromuscular disease," *American Journal of Physical Medicine & Rehabilitation*, vol. 81, Supplement, pp. S108–S120, 2002.

[6] M. P. Davis and D. Walsh, "Mechanisms of fatigue," *The Journal of Supportive Oncology*, vol. 8, no. 4, pp. 164–174, 2010.

[7] L. R. Osternig, "2 Isokinetic Dynamometry," *Exercise and Sport Sciences Reviews*, vol. 14, pp. 45–80, 1986.

[8] L. Vandervelde, P. Y. Van den Bergh, A. Renders, N. Goemans, and J.-L. Thonnard, "Relationships between motor impairments and activity limitations in patients with neuromuscular disorders," *Journal of Neurology, Neurosurgery, and Psychiatry*, vol. 80, no. 3, pp. 326–332, 2009.

[9] K. Dipla, T. Tsirini, A. Zafeiridis et al., "Fatigue resistance during high-intensity intermittent exercise from childhood to adulthood in males and females," *European Journal of Applied Physiology*, vol. 106, no. 5, pp. 645–653, 2009.

[10] P. Gentil, M. H. Campos, S. Soares et al., "Comparison of elbow flexor isokinetic peak torque and fatigue index between men and women of different training level," *European Journal of Translational Myology*, vol. 27, no. 4, p. 7070, 2017.

[11] F. Dupuis, G. Sole, C. Mercier, and J. S. Roy, "Impact of fatigue at the shoulder on the contralateral upper limb kinematics and performance," *PLoS One*, vol. 17, no. 4, article e0266370, 2022.

[12] T. F. Galvão, T. S. A. Pansani, and D. Harrad, "Principais itens para relatar Revisões Sistemáticas e Meta-análises: A recomendação PRISMA," *Epidemiologia e Serviços de Saúde*, vol. 24, no. 2, pp. 335–342, 2015.

[13] G. A. Wells, B. Shea, D. O'Connell et al., "The Newcastle-Ottawa scale (NOS) for assessing the quality of nonrandomized studies in meta-analyses," http://www.ohri.ca/Programs/clinical_epidemiology/oxford.asp.

[14] L. Brauers, E. Rameckers, D. Severijns, P. Feys, R. Smeets, and K. Klingels, "Measuring motor fatigability in the upper limbs in individuals with neurologic disorders: a systematic review," *Archives of Physical Medicine and Rehabilitation*, vol. 101, no. 5, pp. 907–916, 2020.

[15] Ministério da Saúde (Brasil), Secretária de Ciências, Tecnologia e Insumos Estratégicos, and Departamento de Ciência e Tecnologia, *Diretrizes metodológicas: elaboração de revisão sistemática e metanálise de estudos observacionais de estudos comparativos sobre fatores de risco e prognóstico*, Ministério da Saúde, Brasília, 2014.

[16] S. Moola, Z. Munn, C. Tufanaru et al., "Chapter 7: Systematic reviews of etiology and risk," in *JBI Manual for Evidence Synthesis*, E. Aromataris and Z. Munn, Eds., JBI, 2020, https://synthesismanual.jbi.global.

[17] C. J. Symonette, B. V. Watson, W. J. Koopman, M. W. Nicolle, and T. J. Doherty, "Muscle strength and fatigue in patients with generalized myasthenia gravis," *Muscle & Nerve*, vol. 41, no. 3, pp. 362–369, 2010.

[18] L. Vinge and H. Andersen, "Muscle strength and fatigue in newly diagnosed patients with myasthenia gravis," *Muscle & Nerve*, vol. 54, no. 4, pp. 709–714, 2016.

[19] B. Jordan, T. Mehl, T. L. K. Schweden, U. Menge, and S. Zierz, "Assessment of physical fatigability and fatigue perception in myasthenia gravis," *Muscle & Nerve*, vol. 55, no. 5, pp. 657–663, 2017.

[20] S. Baldanzi, G. Ricci, M. Bottari, L. Chico, C. Simoncini, and G. Siciliano, "The proposal of a clinical protocol to assess central and peripheral fatigue in myotonic dystrophy type 1," *Archives Italiennes de Biologie*, vol. 155, no. 1-2, pp. 43–53, 2017.

[21] F. Menotti, I. Bazzucchi, F. Felici, A. Damiani, M. C. Gori, and A. Macaluso, "Neuromuscular function after muscle fatigue in Charcot-Marie-Tooth type 1A patients," *Muscle & Nerve*, vol. 46, no. 3, pp. 434–439, 2012.

[22] L. P. Lowes, L. N. Alfano, B. A. Yetter et al., "Proof of concept of the ability of the kinect to quantify upper extremity function in dystrophinopathy," *PLoS Currents*, vol. 5, 2013.

[23] L. El Mhandi and F. Bethoux, "Isokinetic testing in patients with neuromuscular diseases: a focused review," *American Journal of Physical Medicine & Rehabilitation*, vol. 92, no. 2, pp. 163–178, 2013.

[24] D. J. Hewson, J. Duchêne, and J. Y. Hogrel, "Changes in impedance at the electrode-skin interface of surface EMG electrodes during long-term EMG recordings," in *2001 Conference Proceedings of the 23rd Annual International Conference of the IEEE Engineering in Medicine and Biology Society*, pp. 3345–3348, Istanbul, Turkey, 2001.

[25] K. Masuda, T. Masuda, T. Sadoyama, M. Inaki, and S. Katsuta, "Changes in surface EMG parameters during static and dynamic fatiguing contractions," *Journal of Electromyography and Kinesiology*, vol. 9, no. 1, pp. 39–46, 1999.

[26] J. V. Basmajian and C. J. de Luca, *Muscle Alive: Their Functions Revealed by Electromyography*, Willians & Wilkins, Baltimore, MD, USA, 1985.

[27] A. D. Vigotsky, I. Halperin, G. J. Lehman, G. S. Trajano, and T. M. Vieira, "Interpreting signal amplitudes in surface electromyography studies in sport and rehabilitation sciences," *Frontiers in Physiology*, vol. 8, p. 985, 2017.

[28] B. M. Haward and M. J. Griffin, "Repeatability of grip strength and dexterity tests and the effects of age and gender," *International Archives of Occupational and Environmental Health*, vol. 75, no. 1, pp. 111–119, 2002.

[29] J. Iriarte and P. de Castro, "Correlation between symptom fatigue and muscular fatigue in multiple sclerosis," *European Journal of Neurology*, vol. 5, no. 6, pp. 579–585, 1998.

[30] K. Pavan, K. Schmidt, T. de Ambrosio Ariça, M. F. Mendes, C. P. Tilbery, and S. Lianza, "Fatigability evaluation on multiple sclerosis patients by using a hand held dynamometer," *Arquivos de Neuro-Psiquiatria*, vol. 64, no. 2a, pp. 283–286, 2006.

[31] A. T. White, J. N. Lee, A. R. Light, and K. C. Light, "Brain activation in multiple sclerosis: a BOLD fMRI study of the effects

of fatiguing hand exercise," *Multiple Sclerosis*, vol. 15, no. 5, pp. 580–586, 2009.

[32] D. J. Mattos, S. C. Domenech, N. J. Borges Junior, and M. J. Santos, "Effect of fatigue on grip force control during object manipulation in carpal tunnel syndrome," *Motor Control*, vol. 16, no. 4, pp. 521–536, 2012.

[33] R. J. Lemmens, Y. J. Janssen-Potten, A. A. Timmermans, A. Defesche, R. J. Smeets, and H. A. Seelen, "Arm hand skilled performance in cerebral palsy: activity preferences and their movement components," *BMC Neurology*, vol. 14, no. 52, 2014.

[34] D. Severijns, I. Lamers, L. Kerkhofs, and P. Feys, "Hand grip fatigability in persons with multiple sclerosis according to hand dominance and disease progression," *Journal of Rehabilitation Medicine*, vol. 47, no. 2, pp. 154–160, 2015.

[35] D. Severijns, M. Lemmens, R. Thoelen, and P. Feys, "Motor fatigability after low-intensity hand grip exercises in persons with multiple sclerosis," *Multiple Sclerosis and Related Disorders*, vol. 10, pp. 7–13, 2016.

[36] M. H. Brooke, "A selective review of muscular dystrophies," in *Annual Educational Program of the American Academy of Neurology. Update on Neuromuscular Diseases*, Toronto, Canada, 1999.

[37] C. F. Aquino, D. V. Vaz, R. S. Brício, P. L. P. Silva, J. M. Ocarino, and S. T. Fonseca, "A Utilização da Dinamometria Isocinética nas Ciências do Esporte e Reabilitação," *Revista Brasileira de Ciência e Movimento*, vol. 15, no. 1, pp. 93–100, 2007.

[38] M. De Ste Croix, M. Deighan, and N. Armstrong, "Assessment and interpretation of isokinetic muscle strength during growth and maturation," *Sports Medicine*, vol. 33, no. 10, pp. 727–743, 2003.

[39] K. Woods, P. Bishop, and E. Jones, "Warm-up and stretching in the prevention of muscular injury," *Sports Medicine*, vol. 37, no. 12, pp. 1089–1099, 2007.

[40] R. M. R. Dias, E. S. Cyrino, E. P. Salvador et al., "Influência do processo de familiarização para avaliação da força muscular em testes de 1-RM," *Revista Brasileira de Medicina do Esporte*, vol. 11, no. 1, pp. 34–38, 2005.

[41] T. S. Ellenbecker and E. P. Roetert, "Concentric isokinetic quadricep and hamstring strength in elite junior tennis players," *Isokinetics and Exercise Science*, vol. 5, no. 1, pp. 3–6, 1995.

[42] E. Kellis, S. Kellis, V. Gerodimos, and V. Manou, "Reliability of isokinetic concentric and eccentric strength in circumpubertal soccer players," *Pediatric Exercise Science*, vol. 11, no. 3, pp. 218–228, 1999.

[43] D. H. Perrin, *Exercício isocinético e avaliação*, Human Kinetics, Champaign, IL, USA, 1993.

[44] V. Baltzopoulos and E. Kellis, "Isokinetic strength during childhood and adolescence," *Pediatric Anaerobic Performance*, E. Praagh, Ed., pp. 225–240, Human Kinetics, 1998.

[45] C. Belkhiria, G. De Marco, and T. Driss, "Effects of verbal encouragement on force and electromyographic activations during exercise," *The Journal of Sports Medicine and Physical Fitness*, vol. 58, no. 5, pp. 750–757, 2018.