Journal of Statistics on Health Decision

EXTENDED ABSTRACT

A6 Cardiac, skeletal and respiratory methods and outcome measures of choice to evaluate muscle strength of patients with Myotonic Dystrophy Type 1: A review.

Tiago Mateus[1], Adriana Costa[1], Diana Viegas[1], Alda Marques[2], Maria T. Herdeiro[1], Sandra Rebelo[1]

[1]Institute of Biomedicine (iBiMED), Department of Medical Sciences, University of Aveiro, 3810-193 Aveiro, Portugal
[2]Institute of Biomedicine (iBiMED), Respiratory Research and Rehabilitation Laboratory – Lab3R, School of Health Sciences (ESSUA), University of Aveiro, Aveiro, Portugal

Introduction

Myotonic dystrophy type 1 (DM1) is the most common form of muscular dystrophy in adults with a prevalence of 1 in 3,000 to 8,000 individuals worldwide [1,2]. DM1 is an autosomal dominant hereditary disease caused by the abnormal expansion of unstable repetitions of cytosine-thymine-guanine trinucleotide (CTG) in the 3' untranslated region of *Myotonic Dystrophy Protein Kinase (DMPK)* gene and present different phenotypes according to the age of onset and length of CTG repeat expansion [3,4].

DM1 is characterized by myotonia, progressive peripheral muscle weakness and other multisystemic alterations, [5–9], with respiratory and cardiac muscle dysfunctions being the most prevalent, in this population, leading to a mortality of 51% to 76% and 30%, respectively. Respiratory and cardiac dysfunction are therefore first and second most common causes of death among adult patients with DM1 [10,11]. Considering that muscle strength measurements are crucial to manage DM1 skeletal (e.g., myotonia, progressive distal muscle weakness, muscle pain, and muscle atrophy) [3,4,11], cardiac and respiratory muscle dysfunction (Figure 1), understanding which outcome measures are the most frequently used to assess muscle strength in DM1 is important for further DM1 studies. Nevertheless, consensual guidance on this matter is somewhat limited due to heterogeneous outcome measures used (Figure 1) [12]. Therefore, this review aimed to gather information about the most frequent outcome measures used to assess muscle strength in adult patients with DM1 to contribute for future clinical practice guidance and research.

Methods:

Search Strategy

This review was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) checklist for systematic reviews and meta-analysis [13–15]. We searched Pubmed, Web of Science and Embase databases with weekly automatic updates retrieved from the date of submission of the present work. Studies using measures of muscle strength assessment in adult patients with DM1 were included (Figure 1)..

Data extraction, synthesis, and analysis

We extracted and gathered data from the included studies assessing muscle strength of cardiac, skeletal and respiratory muscles, number of participants (patients and controls), age and sex, CTG repeat length, measures and main findings. Data regarding age, sex, CTG repeat length, body mass index and degree of muscle impairment were collected to characterize the population. All data gathered helped to draw conclusion regarding the patients with DM1 and controls characterization and to understand what outcome measures were the most frequently used to assess cardiac, skeletal and respiratory muscle strength.

Results

Participants characterization

From a total of 80 included studies a total of 5204 patients with DM1 were included. Sample size ranged from 6 to 406 patients. Participants were 43±4 (mean±SD) years old (31-53), equally represented in terms of sex (50.3% female and 49.7% male) and within normal body mass index values (25±2 kg/m^2 [19.5-29 kg/m^2]) although 38 studies did not report the weight measurements. The reported CTG repeat length of patients, mainly evaluated through peripheral blood leukocytes, was 647±211 repeats (387-1338), although 53 studies did not report a mean of CTG repeat length. Muscle Impairment Rating Scale (MIRS)

Keywords:
Myotonic dystrophy type 1, respiratory muscle strength, cardiac muscle strength, skeletal muscle strength, outcome measures, muscle strength, echocardiography, quantitative muscle test, manometry

Corresponding author:
Sandra Rebelo
srebelo@ua.pt

Conflict of interest:
The authors declare no conflict of interests.

First published: 22JUN2021

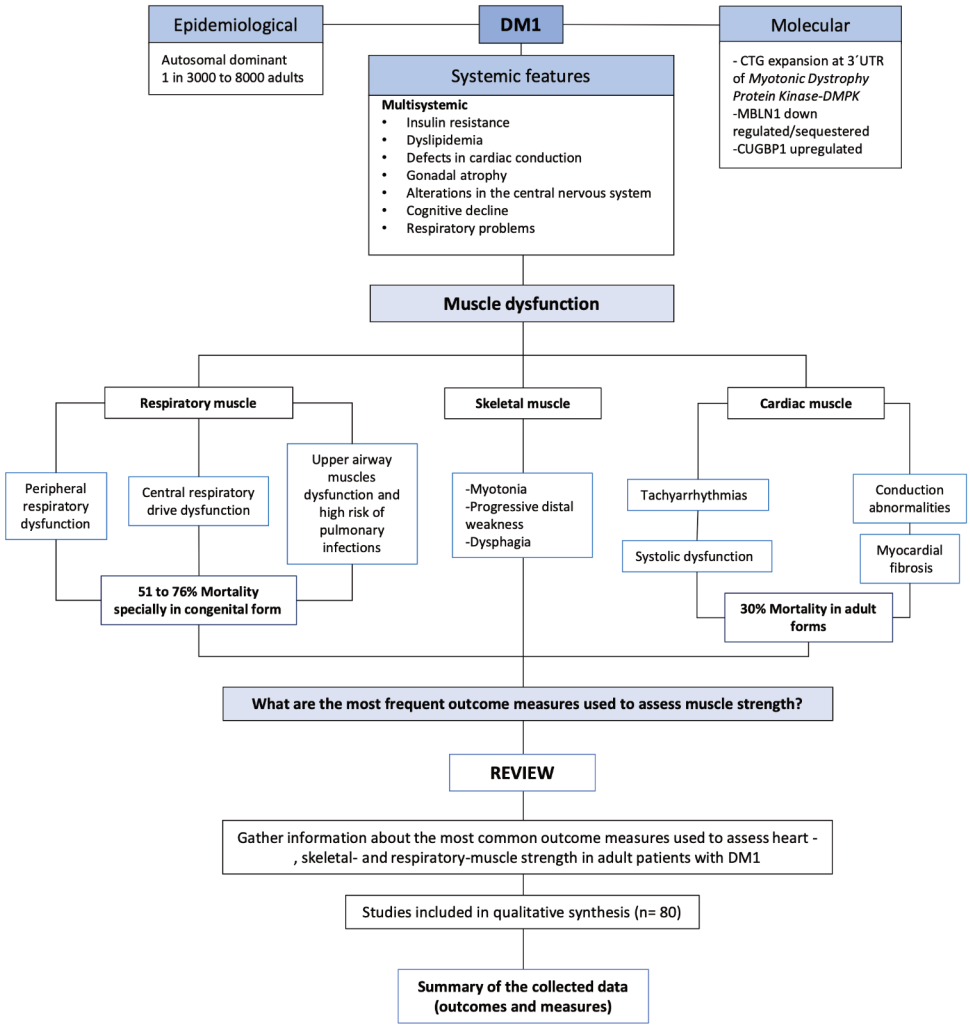

Figure 1 - Schematic representation of epidemiological, molecular and systemic features of Myotonic Dystrophy type 1 (DM1). The muscle dysfunctions previously associated to DM1 were also summarized. Upon literature revision one important question raised and was the basis for the present literature review. The latter includes 80 studies.

grades I-III was reported in 996 patients with DM1, and IV-V was reported in 1064 patients with DM1, with 45 of included studies did not report the use of this scale.

Twenty-six studies compared patients with DM1 with healthy controls. In total, 743 healthy volunteers were included. Sample sizes ranged from 6 to 71. Healthy volunteers were 40±3 years old (32 to 50) equally represented in terms of sex (45.9% female and 54.1% male) and normal weight (body mass index = 23±1 kg/m2 [20 to 26 kg/m^2]), although this variable was not reported in 16 studies.

Cardiac Muscle strength

Twenty-four studies indirectly measured cardiac muscle strength [16-39]. From these, 22 studies used echocardiography [16-19,21,23-34,36,37,39,40] and 3 used cardiac magnetic resonance [20,35,37] (Figure 2). The echocardiography studies mostly evaluated left ventricular ejection fraction (n=21) [16-19,21,23-34,36,37,39,40]. Left ventricular ejection fraction values of patients with DM1 ranged from 56%-70% and 61%-77% for controls [16-19,21,23-34,36,37,39,40]. Further, cardiac magnetic resonance studies were also performed, and the left ventricular ejection fraction was also the most used measure (n=3) (Figure 2). Patients with DM1 had a median of 58% [35] and mean 57.6±8% [20] for left ventricular ejection fraction and the control group had a mean value of 59.12±6% [20].

Skeletal muscle strength

From the 45 studies assessed skeletal muscle strength, 39 used quantitative muscle testing [41-68] and fifteen used manual muscle testing [35,37-40,43,51,59,60,66,67,69-71] (Figure 2).

Manual muscle testing assessed the strength of ankle dorsiflexors [37,43,51,60,69], ankle plantar flexors [43,51], back extensors [69], elbow extensors [43,51,69], elbow flexors [43,51,69], grip strength [37], hip flexors [43,51,60,69], knee extensors [43,51,60,69], knee flexors [43,60,69], neck flexors [43,69],

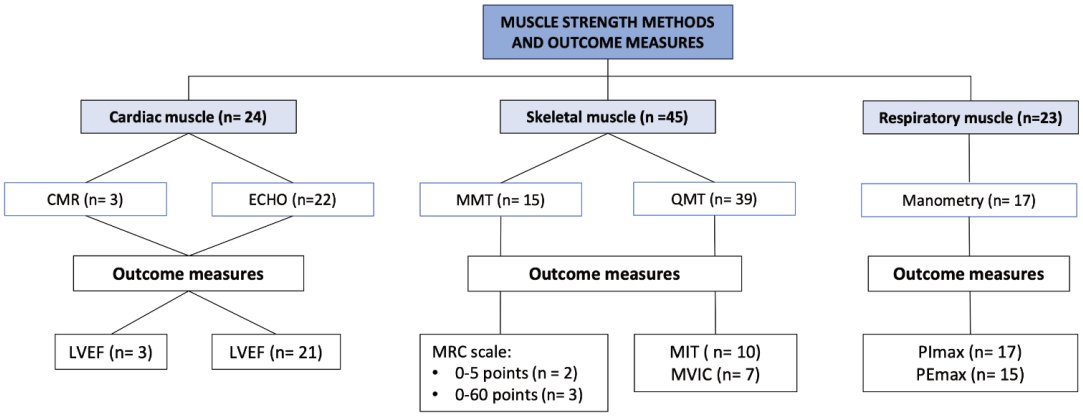

Figure 2 - Muscle strength (cardiac, skeletal and respiratory) methods and outcome measure frequently used in the gathered studies. Abbreviations: CMR- Cardiac Magnetic Resonance; ECHO- Echocardiography; LVEF- Left Ventricular Ejection Fraction; MMT- Manual Muscle Testing; QMT- Quantitative Muscle Testing; MRC- Medical Research Council; MVIC- Maximal Voluntary Isometric Contraction; MIT- Maximum Isometric Torque; PImax- Maximal Inspiratory Pressure; PEmax- Maximal Expiratory Pressure;

shoulder abductors [43,51,69], trunk extensors [38], trunk flexors [38,69], wrist extensors [43,50,69] and total muscle groups [35,36,39,40,50,59,66,67,70,71].

Concerning manual muscle testing results in patients with DM1, there was a preference in using MRC scale between 0 to 5 points [43,59] and 0-60 points [39,40,71] in patients with DM1 (Figure 2).

From the 39 studies that used quantitative muscle testing, the most used measures were maximum isometric torque (n= 10) [41,49,50,56–58,65,72,73] and maximal voluntary isometric contraction (n=7) [42,43,46,53,59,74,75] (Figure 2). Seventeen studies did not report the method used [45,54,55,56,59,61-65,67,68,73,76-79].

Quantitative muscle testing assessed the strength of ankle dorsiflexors [45,54], grip [43,45,55,56,59,62-64,67,73,78,79], hip flexors [45,54], knee extensors [45,54], lip strength [68], maximum bit strength [77], pinch [56,62,63,73], tongue [76] and wrist extensors [45]. Muscle strength results in patients with DM1 using quantitative muscle test ranged between 14 and 47.8 lb [45,54], 5.2 and 12.8 kg [55,56,59,61,62,64,73,78], 12 N and 82.6 N [68,77], 31.7% and 41.3% of predicted [61,64] and a mean of 132 kPa [76]. In controls the muscle test results were 2.5 kg [59] and 29 N [68].

Maximal voluntary isometric contraction assessed the strength of Abductor digiti minimi [42], ankle dorsiflexors [46,75], ankle plantar flexors [75], grip [44,53,74], elbow flexors [59], elbow extensors [59], hip abductors [75], hip extensors [75], knee extensors [46,59,75], knee flexors [59,75] and pinch [44]. The results ranged between 42.2 N and 303 N [44,46,74,75] in patients with DM1 and between 143.7 N and 371.5 N [46,74,75] in controls.

Maximum isometric torque assessed the strength of ankle dorsiflexors [41,49,50,52,56–58,72,73], ankle evertors [49,50], ankle plantar flexors [41,57,58], elbow extensors [72], elbow flexors [72], hip extensors [57,58], hip flexors [41,56–58,72], knee extensors [41,56–58,65,72,73] knee flexors [56–58,72], lower limb [56], neck flexors [41], shoulder abductors [72,73], and wrist extensors [72]. The results ranged between 5.1 N and 139.78 N [41,56–58,72,73] in patients with DM1 and 19.7 Nm and 129.4 Nm [41,56–58,72,73] in controls.

Respiratory Muscle Strength

From the 23 studies that measured respiratory muscle strength, 17 used manometry [71,73,79-93] (Figure 2). Through manometry there was a preference in using maximal expiratory pressure (n=15) [73,79-85,87-93] and maximal inspiratory pressure (n=17) [71,73,79-93] (Figure 2). Maximal expiratory pressure mean values ranged between 35.5 cmH2O and 71 cmH2O in patients with DM1 and controls presented a mean value of 133.8±28 cmH2O [73,79,80,82-84,88-93]. Maximal inspiratory pressure mean values ranged between 34 and 76 cmH2O in patients with DM1 and controls presented a mean value of 77.8±44 cmH2O [73,79,80,82-84,88-93].

Discussion

In the current literature there was a high variability and heterogeneity regarding the outcome measures used to assess muscle strength in patients with DM1, as also reported in previous studies protocols and methods referring it as a limitation [94–96]. Therefore, it was necessary to gather and review the most frequent outcome measures to understand which outcome measures are more frequently used to evaluate muscle strength in patients with DM1.

Our results clearly indicated a preference of echocardiography over cardiac magnetic resonance to evaluate cardiac strength, but previous studies [97,98] showed that cardiac magnetic resonance is more reproducible and accurate to evaluate left ventricular volume and ejection fraction than echocardiography. Further, echocardiography is thought to underestimate left ventricular ejection fraction values compared with cardiac magnetic resonance [97,98]. Echocardiography may have been more often used due to its lower cost compared to cardiac magnetic resonance procedure which is significantly higher [97]. In overall, the ejection fraction was the most used measure to indirectly evaluate cardiac muscle strength. However, more evidence is needed to compare the left ventricular ejection fraction between patients with DM1 and matched controls, and to clearly understand the differences between echocardiography and cardiac magnetic resonance in patients with DM1.

Regarding skeletal muscle strength, quantitative muscle test and manual muscle test were a frequently used method, although manual muscle test has its limitations, since the tester judgment and strength are subjective and can influence the results [94,95]. This limitation does not happen in quantitative muscle test, since it is a more precise method of muscle strength assessment and discrimination, between healthy and patients with DM1 with different levels of impairment [94,95].

Although 17 studies did not report the methodology for their quantitative muscle testing, the measures of maximum isometric force, maximal voluntary isometric contraction and maximum isometric torque were consistently used [45,54,55,56,59,61-65,67,68,73,76-79], with the latter being the most reported skeletal-muscle measure in this review. Grip strength was also frequently used among examiners and may be a suitable measure to evaluate and discriminate patients with DM1 according to severity. The results revealed the preference of muscle isometric torque, maximal voluntary isometric contraction and grip strength as measures to evaluate muscle strength/weakness progression and may be considered in future observational studies and in clinical practice.

Lastly, regarding respiratory muscle strength, examiners demonstrated a preference for the use maximal inspiratory and expiratory pressure measures. However, there are some facts to be considered regarding maximal inspiratory pressure, since in previous studies, maximal inspiratory pressure has been reported to lead to falsely low values in patients with neuromuscular disorders, due to the challenges of maintaining the mouth seal and keeping maximal inspiratory effort [99]. To overcome this challenge, sniff nasal inspiratory pressure could be used to evaluate inspiratory and diaphragm muscle strength since it is non-invasive and easier to perform by patients with low levels of coordination [94,99–101]. In addition, a significant decrease in sniff nasal inspiratory pressure was observed in 2 studies in patients with DM1 compared with the control group [71,83].

This review has many strengths including a systematic search of three databases (Web of Science, PubMed and Embase) and a broad range of search keywords, resulting in a wide selection of studies according to the PRISMA guidelines methodology.

Some limitations of this review are the: (i) inclusion of peer-reviewed publications exclusively; (ii) exclusion of interventional studies; (iii) Presence of some degree of bias when performing the qualitative assessment of studies.; (iv) absence of correlation between cardiac, skeletal, and respiratory muscle strength due to high heterogeneity and lack of patient characterization.

Conclusion

We successfully gathered the more frequent outcome measures that evaluate muscle strength in patients with DM1. Echocardiography and left ventricular ejection fraction were the preferential method and indirect measure for cardiac muscle strength, respectively. For skeletal-muscle strength, the researchers preferentially used quantitative and manual muscle strength methods, grip strength, maximum isometric torque, maximal voluntary isometric contraction and the medical research council (0-5 points and 0-60 points) scale were the most frequent used measures. Through manometry, maximal expiratory pressure and maximal inspiratory pressure were the measures of choice to evaluate respiratory muscle strength.

The results of this review were of utmost importance since muscle strength evaluation is essential to correctly assess disease severity and response to interventions that aim to improve muscle strength in patients with DM1. Clinicians and researchers should consider using the same methodologies and outcome measures described in this review, to contribute to a better understanding of the response in muscle strength in future clinical trials and interventions, and thus contributing to a higher quality research of this disease. Further, a Core Outcome Set to assess muscle strength for the management of patients with DM1 is also urgently needed.

Acknowledgements

This research was funded by the Institute of Biomedicine (iBiMED)—UID/BIM/04501/2020 and by the MEDISIS project (CENTRO-01-0246-FEDER-000018).

References

1. Day JW, Ranum LPW. RNA pathogenesis of the myotonic dystrophies. Neuromuscul Disord. 2005 Jan;15(1):5–16.
2. Ashizawa T, Gagnon C, Groh WJ, Gutmann L, Johnson NE, Meola G, Moxley R, Pandya S, Rogers MT, Simpson E, Angeard N, Bassez G, Berggren KN, Bhakta D, Bozzali M, Broderick A, Byrne JLB, Campbell C, Cup E, Day JW, De Mattia E, Duboc D, Duong T, Eichinger K, Ekstrom A-B, van Engelen B, Esparis B, Eymard B, Ferschl M, Gadalla SM, Gallais B, Goodglick T, Heatwole C, Hilbert J, Holland V, Kierkegaard M, Koopman WJ, Lane K, Maas D, Mankodi A, Mathews KD, Monckton DG, Moser D, Nazarian S, Nguyen L, Nopoulos P, Petty R, Phetteplace J, Puymirat J, Raman S, Richer L, Roma E, Sampson J, Sansone V, Schoser B, Sterling L, Statland J, Subramony SH, Tian C, Trujillo C, Tomaselli G, Turner C, Venance S, Verma A, White M, Winblad S. Consensus-based care recommendations for adults with myotonic dystrophy type 1. Neurol Clin Pract [Internet]. 2018 Dec;8(6):507–20. Available from: http://cp.neurology.org/lookup/doi/10.1212/CPJ.0000000000000531
3. Wenninger S, Montagnese F, Schoser B. Core Clinical Phenotypes in Myotonic Dystrophies. Front Neurol. 2018 May;9.
4. Liu Q, Zheng Y-F, Zhu Y-P, Ling S-Q, Li W-R. Clinical, pathological and genetic characteristics of a pedigree with myotonic dystrophy type 1. Exp Ther Med. 2015 Nov;10(5):1931–6.
5. Mateus T, Martins F, Nunes A, Herdeiro MT, Rebelo and S. Metabolic Alterations in Myotonic Dystrophy Type 1 and Their Correlation with Lipin. Int J Environ Res Public Health [Internet]. 2021 Feb 12;18(4):1794. Available from: https://www.mdpi.com/1660-4601/18/4/1794
6. Mateus T, Almeida I, Costa A, Viegas D, Magalhães S, Martins F, Herdeiro MT, da Cruz e Silva OAB, Fraga C, Alves I, Nunes A, Rebelo S. Fourier-Transform Infrared Spectroscopy as a Discriminatory Tool for Myotonic Dystrophy Type 1 Metabolism: A Pilot Study. Int J Environ Res Public Health [Internet]. 2021 Apr 6;18(7):3800. Available from: https://www.mdpi.com/1660-4601/18/7/3800
7. Johnson NE. Myotonic Muscular Dystrophies. Contin Lifelong Learn Neurol [Internet]. 2019 Dec;25(6):1682–95. Available from: http://journals.lww.com/10.1212/CON.0000000000000793
8. Bozovic I, Peric S, Pesovic J, Bjelica B, Brkusanin M, Basta I, Bozic M, Sencanic I, Marjanovic A, Brankovic M, Savic-Pavicevic D, Rakocevic-Stojanovic V. Myotonic Dystrophy Type 2 – Data from the Serbian Registry. J Neuromuscul Dis [Internet]. 2018 Oct 23;5(4):461–9. Available from: https://www.medra.org/servlet/aliasResolver?alias=iospress&doi=10.3233/JND-180328
9. Yum K, Wang ET, Kalsotra A. Myotonic dystrophy: disease repeat range, penetrance, age of onset, and relationship between repeat size and phenotypes. Curr Opin Genet Dev [Internet]. 2017 Jun;44:30–7. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0959437X16301459
10. Mathieu J, Allard P, Potvin L, Prevost C, Begin P. A 10-year study of mortality in a cohort of patients with myotonic dystrophy. Neurology. 1999 May;52(8):1658–1658.
11. Sansone VA, Gagnon C. 207th ENMC Workshop on chronic respiratory insufficiency in myotonic dystrophies: Management and implications for research, 27–29 June 2014, Naarden, The Netherlands. Neuromuscul Disord. 2015 May;25(5):432–42.
12. Kirkham JJ, Gorst S, Altman DG, Blazeby JM, Clarke M, Tunis S, Williamson PR. Core Outcome Set-STAndardised Protocol Items: the COS-STAP Statement. Trials. 2019 Dec;20(1):116.
13. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, Shamseer L, Tetzlaff JM, Akl EA, Brennan SE, Chou R, Glanville J, Grimshaw JM, Hróbjartsson A, Lalu MM, Li T, Loder EW, Mayo-Wilson E, McDonald S, McGuinness LA, Stewart LA, Thomas J, Tricco AC, Welch VA, Whiting P, Moher D. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ [Internet]. 2021 Mar 29;n71. Available from: https://www.bmj.com/lookup/doi/10.1136/bmj.n71
14. Salameh J-P, Bossuyt PM, McGrath TA, Thombs BD, Hyde CJ, Macaskill P, Deeks JJ, Leeflang M, Korevaar DA, Whiting P, Takwoingi Y, Reitsma JB, Cohen JF, Frank RA, Hunt HA, Hooft L, Rutjes AWS, Willis BH, Gatsonis C, Levis B, Moher D, McInnes MDF. Preferred reporting items for systematic review and meta-analysis of diagnostic test accuracy studies (PRISMA-DTA): explanation, elaboration, and checklist. BMJ [Internet]. 2020 Aug 14;m2632. Available from: https://www.bmj.com/lookup/doi/10.1136/bmj.m2632
15. Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gøtzsche PC, Ioannidis JPA, Clarke M, Devereaux PJ, Kleijnen J, Moher D. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. J Clin Epidemiol [Internet]. 2009 Oct;62(10):e1–34. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0895435609001802
16. Bhakta D, Groh MR, Shen C, Pascuzzi RM, Groh WJ. Increased mortality with left ventricular systolic dysfunction and heart failure in adults with myotonic dystrophy type 1. Am Heart J. 2010 Dec;160(6):1137-1141.e1.
17. Bhakta D, Lowe MR, Groh WJ. Prevalence of structural cardiac abnormalities in patients with myotonic dystrophy type I. Am Heart J. 2004 Feb;147(2):224–7.
18. Bienias P, Łusakowska A, Ciurzyński M, Rymarczyk Z, Irzyk K, Konwerski M, Ciąpała K, Kowalski P, Kamińska A, Pruszczyk P. Cardiac autonomic function in type 1 and type 2 myotonic dystrophy. Clin Auton Res. 2017 Jun;27(3):193–202.
19. Bienias P, Łusakowska A, Ciurzyński M, Rymarczyk Z, Irzyk K, Kurnicka K, Kamińska A, Pruszczyk P. Supraventricular and Ventricular Arrhythmias Are Related to the Type of Myotonic Dystrophy but Not to Disease Duration or Neurological Status. Pacing Clin Electrophysiol. 2016 Sep;39(9):959–68.
20. Choudhary P, Nandakumar R, Greig H, Broadhurst P, Dean J, Puranik R, Celermajer DS, Hillis GS. Structural and electrical cardiac abnormalities are prevalent in asymptomatic adults with myotonic dystrophy. Heart. 2016 Sep;102(18):1472–8.
21. Di Cori A, Bongiorni MG, Zucchelli G, Soldati E, Falorni M, Segreti L, Gemignani C, Siciliano A, Bovenzi FM, Di Bello V. Early Left Ventricular Structural Myocardial Alterations and Their Relationship with Functional and Electrical Properties of the Heart in Myotonic Dystrophy Type 1. J Am Soc Echocardiogr. 2009 Oct;22(10):1173–9.
22. Fayssoil A, Nardi O, Annane D, Orlikowski D. Diastolic function in Steinert's disease. Neurol Int. 2014 Mar;6(1).
23. Fung KC, Corbett A, Kritharides L. Myocardial tissue velocity reduction is correlated with clinical neurologic severity in myotonic dystrophy. Am J Cardiol. 2003 Jul;92(2):177–81.
24. Garcia R, Rehman M, Goujeau C, Degand B, Le Gal F, Stordeur B, Labarre Q, Christiaens L, Bouleti C. Left ventricular longitudinal strain impairment predicts cardiovascular events in asymptomatic type 1 myotonic dystrophy. Int J Cardiol. 2017 Sep;243:424–30.
25. Garcia R, Labarre Q, Degand B, Ingrand P, Le Gal F, Bonnet B, Delaubier A, Guillou C, Gellen B, Coisne D, Bouleti C, Christiaens L. Apical left ventricular myocardial dysfunction is an early feature of cardiac involvement in myotonic dystrophy type 1. Echocardiography. 2017 Feb;34(2):184–90.

26. Guedes H, Moreno N, dos Santos RP, Marques L, Seabra D, Pereira A, Andrade A, Pinto P. Importance of three-dimensional speckle tracking in the assessment of left atrial and ventricular dysfunction in patients with myotonic dystrophy type 1. Rev Port Cardiol [Internet]. 2018 Apr;37(4):333–8. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0870255117303773
27. Gomes L, Pereira T, Martins L. Perfil cardiovascular na distrofia muscular miotónica tipo 1: estudo de uma série de casos seguida num centro especializado. Rev Port Cardiol. 2014 Dec;33(12):765–72.
28. Lindqvist P, Mörner S, Olofsson BO, Backman C, Lundblad D, Forsberg H, Henein MY. Ventricular dysfunction in type 1 myotonic dystrophy: Electrical, mechanical, or both? Int J Cardiol. 2010 Sep;143(3):378–84.
29. Ozyigit T, Ozben B, Oflaz H, Serdaroglu P. Evaluation of Biventricular Functions With Tissue Doppler Imaging in Patients With Myotonic Dystrophy. Clin Cardiol. 2010 Mar;33(3):126–31.
30. Parisi M, Galderisi M, Sidiropulos M, Fiorillo C, Lanzillo R, D'Errico A, Grieco M, Innelli P, Santoro L, de Divitiis O. Early detection of biventricular involvement in myotonic dystrophy by tissue Doppler. Int J Cardiol. 2007 May;118(2):227–32.
31. Paunic T, Peric S, Cvitan E, Raspopovic S, Peric M, Mandic Stojmenovic G, Rakocevic Stojanovic V. Routine echocardiography in patients with myotonic dystrophy type 1. J Chinese Med Assoc. 2017 Jul;80(7):408–12.
32. Russo V, Di Meo F, Rago A, Papa AA, Molino A, Mosella M, Politano L, Russo MG, Nigro G. Paroxysmal atrial fibrillation in myotonic dystrophy type 1 patients: P wave duration and dispersion analysis. Eur Rev Med Pharmacol Sci. 2015 Apr;19(7):1241–8.
33. Russo V, Papa AA, Rago A, D'Ambrosio P, Cimmino G, Palladino A, Politano L, Nigro G. Increased heterogeneity of ventricular repolarization in myotonic dystrophy type 1 population. Acta Myol myopathies cardiomyopathies Off J Mediterr Soc Myol. 2016 Oct;35(2):100–6.
34. Russo V, Rago A, Ciardello C, Russo MG, Calabrò P, Politano L, Nigro G. The Role of the Atrial Electromechanical Delay in Predicting Atrial Fibrillation in Myotonic Dystrophy Type 1 Patients. J Cardiovasc Electrophysiol. 2016 Jan;27(1):65–72.
35. Hermans MC, Faber CG, Bekkers SC, de Die-Smulders CE, Gerrits MM, Merkies IS, Snoep G, Pinto YM, Schalla S. Structural and functional cardiac changes in myotonic dystrophy type 1: a cardiovascular magnetic resonance study. J Cardiovasc Magn Reson [Internet]. 2012 Dec 24;14(1):48. Available from: https://jcmr-online.biomedcentral.com/articles/10.1186/1532-429X-14-48
36. Meola G, Sansone V, Marinou K, Cotelli M, Moxley R., Thornton C., De Ambroggi L. Proximal myotonic myopathy: a syndrome with a favourable prognosis? J Neurol Sci. 2002 Jan;193(2):89–96.
37. Petri H, Ahtarovski KA, Vejlstrup N, Vissing J, Witting N, Køber L, Bundgaard H. Myocardial fibrosis in patients with myotonic dystrophy type 1: a cardiovascular magnetic resonance study. J Cardiovasc Magn Reson. 2014 Dec;16(1):59.
38. Solbakken G, Bjørnaå B, Kirkhus E, Nguyen B, Hansen G, Frich JC, Ørstavik K. MRI of trunk muscles and motor and respiratory function in patients with myotonic dystrophy type 1. BMC Neurol. 2019 Dec;19(1):135.
39. Park D, Park J-S. Quantitative Assessment of Trunk Muscles Involvement in Patients with Myotonic Dystrophy Type 1 Using a Whole Body Muscle Magnetic Resonance Imaging. Eur Neurol. 2017;77(5–6):238–45.
40. Park J-S, Kim N, Park D. Diastolic heart dysfunction is correlated with CTG repeat length in myotonic dystrophy type 1. Neurol Sci. 2018 Nov;39(11):1935–43.
41. Bachasson D, Moraux A, Ollivier G, Decostre V, Ledoux I, Gidaro T, Servais L, Behin A, Stojkovic T, Hébert LJ, Puymirat J, Eymard B, Bassez G, Hogrel J-Y. Relationship between muscle impairments, postural stability, and gait parameters assessed with lower-trunk accelerometry in myotonic dystrophy type 1. Neuromuscul Disord. 2016 Jul;26(7):428–35.
42. Boërio D, Hogrel J-Y, Bassez G, Lefaucheur J-P. Neuromuscular excitability properties in myotonic dystrophy type 1. Clin Neurophysiol. 2007 Nov;118(11):2375–82.
43. Bouchard J-P, Cossette L, Bassez G, Puymirat J. Natural history of skeletal muscle involvement in myotonic dystrophy type 1: a retrospective study in 204 cases. J Neurol. 2015 Feb;262(2):285–93.
44. Cutellè C, Rastelli E, Gibellini M, Greco G, Frezza E, Botta A, Terracciano C, Massa R. Validation of the Nine Hole Peg Test as a measure of dexterity in myotonic dystrophy type 1. Neuromuscul Disord. 2018 Nov;28(11):947–51.
45. DiPaolo G, Jimenez-Moreno C, Nikolenko N, Atalaia A, Monckton DG, Guglieri M, Lochmüller H. Functional impairment in patients with myotonic dystrophy type 1 can be assessed by an ataxia rating scale (SARA). J Neurol. 2017 Apr;264(4):701–8.
46. Esposito F, Cè E, Rampichini S, Monti E, Limonta E, Fossati B, Meola G. Electromechanical delays during a fatiguing exercise and recovery in patients with myotonic dystrophy type 1. Eur J Appl Physiol [Internet]. 2017 Mar 14;117(3):551–66. Available from: http://link.springer.com/10.1007/s00421-017-3558-4
47. Hammarén E, Kjellby-Wendt G, Kowalski J, Lindberg C. Factors of importance for dynamic balance impairment and frequency of falls in individuals with myotonic dystrophy type 1 – A cross-sectional study – Including reference values of Timed Up & Go, 10m walk and step test. Neuromuscul Disord. 2014 Mar;24(3):207–15.
48. Hammarén E, Kjellby-Wendt G, Lindberg C. Muscle force, balance and falls in muscular impaired individuals with myotonic dystrophy type 1: A five-year prospective cohort study. Neuromuscul Disord. 2015 Feb;25(2):141–8.
49. Hébert LJ, Vial C, Hogrel J-Y, Puymirat J. Ankle Strength Impairments in Myotonic Dystrophy Type 1: A Five-Year Follow-up. J Neuromuscul Dis. 2018 Aug;5(3):321–30.
50. Hébert LJ, Remec J-F, Saulnier J, Vial C, Puymirat J. The use of muscle strength assessed with handheld dynamometers as a non-invasive biological marker in myotonic dystrophy type 1 patients: a multicenter study. BMC Musculoskelet Disord. 2010 Dec;11(1):72.
51. Hermans MCE, Faber CG, Vanhoutte EK, Bakkers M, De Baets MH, de Die-Smulders CEM, Merkies ISJ. Peripheral neuropathy in myotonic dystrophy type 1. J Peripher Nerv Syst. 2011 Mar;16(1):24–9.
52. Hiba B, Richard N, Hébert LJ, Coté C, Nejjari M, Vial C, Bouhour F, Puymirat J, Janier M. Quantitative assessment of skeletal muscle degeneration in patients with myotonic dystrophy type 1 using MRI. J Magn Reson Imaging. 2012 Mar;35(3):678–85.
53. Hogrel J-Y. Quantitative myotonia assessment using force relaxation curve modelling. Physiol Meas. 2009 Jul;30(7):719–27.
54. Jimenez-Moreno AC, Nikolenko N, Kierkegaard M, Blain AP, Newman J, Massey C, Moat D, Sodhi J, Atalaia A, Gorman GS, Turner C, Lochmüller H. Analysis of the functional capacity outcome measures for myotonic dystrophy. Ann Clin Transl Neurol. 2019 Jul;acn3.50845.
55. Kierkegaard M, Petitclerc E, Hébert LJ, Gagnon C. Is one trial enough for repeated testing? Same-day assessments of walking, mobility and fine hand use in people with myotonic dystrophy type 1. Neuromuscul Disord. 2017 Feb;27(2):153–8.

56. Kierkegaard M, Petitclerc É, Hébert L, Mathieu J, Gagnon C. Responsiveness of performance-based outcome measures for mobility, balance, muscle strength and manual dexterity in adults with myotonic dystrophy type 1. J Rehabil Med. 2018;50(3):269–77.
57. Knak KL, Sheikh AM, Andersen H, Witting N, Vissing J. Intrarater reliability and validity of outcome measures in myotonic dystrophy type 1. Neurology. 2020 Jun;94(24):e2508–20.
58. Knak KL, Sheikh AM, Witting N, Vissing J. Responsiveness of outcome measures in myotonic dystrophy type 1. Ann Clin Transl Neurol. 2020 Aug;7(8):1382–91.
59. Moxley RT, Logigian EL, Martens WB, Annis CL, Pandya S, Moxley RT, Barbieri CA, Dilek N, Wiegner AW, Thornton CA. Computerized hand grip myometry reliably measures myotonia and muscle strength in myotonic dystrophy (DM1). Muscle Nerve. 2007 Sep;36(3):320–8.
60. Petitclerc É, Hébert LJ, Mathieu J, Desrosiers J, Gagnon C. Lower limb muscle strength impairment in late-onset and adult myotonic dystrophy type 1 phenotypes. Muscle Nerve. 2017 Jul;56(1):57–63.
61. Pruna L, Machado F, Louis L, Vassé G, Kaminsky P. Fonction musculaire et atteinte d'organes dans la dystrophie myotonique de type 1. Rev Neurol (Paris). 2011 Jan;167(1):23–8.
62. Raymond K, Levasseur M, Mathieu J, Desrosiers J, Gagnon C. A 9-year follow-up study of the natural progression of upper limb performance in myotonic dystrophy type 1: A similar decline for phenotypes but not for gender. Neuromuscul Disord. 2017 Jul;27(7):673–82.
63. Raymond K, Auger L-P, Cormier M-F, Vachon C, St-Onge S, Mathieu J, Noreau L, Gagnon C. Assessing upper extremity capacity as a potential indicator of needs related to household activities for rehabilitation services in people with myotonic dystrophy type 1. Neuromuscul Disord. 2015 Jun;25(6):522–9.
64. Rinninella E, Silvestri G, Cintoni M, Perna A, Martorana GE, De Lorenzo A, Rossini PM, Miggiano GAD, Gasbarrini A, Mele MC. Clinical use of bioelectrical impedance analysis in patients affected by myotonic dystrophy type 1: A cross-sectional study. Nutrition. 2019 Nov;67–68:110546.
65. Roussel M-P, Hébert LJ, Duchesne E. Intra-Rater Reliability and Concurrent Validity of Quantified Muscle Testing for Maximal Knee Extensors Strength in Men with Myotonic Dystrophy Type 1. J Neuromuscul Dis. 2019 May;6(2):233–40.
66. Sansone V, Gandossini S, Cotelli M, Calabria M, Zanetti O, Meola G. Cognitive impairment in adult myotonic dystrophies: a longitudinal study. Neurol Sci. 2007 Mar;28(1):9–15.
67. Sedehizadeh S, Brook JD, Maddison P. Body composition and clinical outcome measures in patients with myotonic dystrophy type 1. Neuromuscul Disord. 2017 Mar;27(3):286–9.
68. Sjögreen L, Lohmander A, Kiliaridis S. Exploring quantitative methods for evaluation of lip function. J Oral Rehabil. 2011 Jun;38(6):410–22.
69. Solbakken G, Ørstavik K, Hagen T, Dietrichs E, Naerland T. Major involvement of trunk muscles in myotonic dystrophy type 1. Acta Neurol Scand. 2016 Dec;134(6):467–73.
70. Tieleman AA, Vinke A, van Alfen N, van Dijk JP, Pillen S, van Engelen BGM. Skeletal muscle involvement in myotonic dystrophy type 2. A comparative muscle ultrasound study. Neuromuscul Disord. 2012 Jun;22(6):492–9.
71. Koc F, Atli G, Menziletoglu SY, Kose S. Antioxidant imbalance in the erythrocytes of Myotonic dystrophy Type 1 patients. Arch Biochem Biophys. 2020 Feb;680:108230.
72. Gagnon C, Petitclerc É, Kierkegaard M, Mathieu J, Duchesne É, Hébert LJ. A 9-year follow-up study of quantitative muscle strength changes in myotonic dystrophy type 1. J Neurol. 2018 Jul;265(7):1698–705.
73. Légaré C, Overend G, Guay S-P, Monckton DG, Mathieu J, Gagnon C, Bouchard L. DMPK gene DNA methylation levels are associated with muscular and respiratory profiles in DM1. Neurol Genet. 2019 Jun;5(3):e338.
74. Hogrel J-Y, Ollivier G, Ledoux I, Hébert LJ, Eymard B, Puymirat J, Bassez G. Relationships between grip strength, myotonia, and CTG expansion in myotonic dystrophy type 1. Ann Clin Transl Neurol. 2017 Dec;4(12):921–5.
75. Wiles CM. Falls and stumbles in myotonic dystrophy. J Neurol Neurosurg Psychiatry. 2005 Jul;77(3):393–6.
76. Umemoto G, Furuya H, Arahata H, Sugahara M, Sakai M, Tsuboi Y. Relationship between tongue thickness and tongue pressure in neuromuscular disorders. Neurol Clin Neurosci. 2016 Jul;4(4):142–5.
77. Umemoto G, Nakamura H, Oya Y, Kikuta T. Masticatory dysfunction in patients with myotonic dystrophy (type 1): a 5-year follow-up. Spec Care Dent. 2009 Sep;29(5):210–4.
78. Kierkegaard M, Harms-Ringdahl K, Holmqvist LW, Tollbäck A. Functioning and disability in adults with myotonic dystrophy type 1. Disabil Rehabil. 2011 Jan;33(19–20):1826–36.
79. Pincherle A, Patruno V, Raimondi P, Moretti S, Dominese A, Martinelli-Boneschi F, Pasanisi MB, Canioni E, Salerno F, Deleo F, Spreafico R, Mantegazza R, Villani F, Morandi L. Sleep breathing disorders in 40 Italian patients with Myotonic dystrophy type 1. Neuromuscul Disord. 2012 Mar;22(3):219–24.
80. Boussaïd G, Wahbi K, Laforet P, Eymard B, Stojkovic T, Behin A, Djillali A, Orlikowski D, Prigent H, Lofaso F. Genotype and other determinants of respiratory function in myotonic dystrophy type 1. Neuromuscul Disord. 2018 Mar;28(3):222–8.
81. Calabrese P, Gryspeert N, Auriant I, Fromageot C, Raphaël J-C, Lofaso F, Benchetrit G. Postural breathing pattern changes in patients with myotonic dystrophy. Respir Physiol. 2000 Aug;122(1):1–13.
82. De Mattia E, Lizio A, Falcier E, Sannicolò G, Gualandris M, Rossi G, Zanolini A, Pozzi S, Messina S, Sframeli M, Lunetta C, Rao F, Sansone VA. Screening for early symptoms of respiratory involvement in myotonic dystrophy type 1 using the Respicheck questionnaire. Neuromuscul Disord. 2020 Apr;30(4):301–9.
83. Evangelista M de A, Dias FAL, Dourado Júnior MET, do Nascimento GC, Sarmento A, Gualdi LP, Aliverti A, Resqueti V, Fregonezi GA de F. Noninvasive assessment of respiratory muscle strength and activity in Myotonic dystrophy. Artero R, editor. PLoS One. 2017 Jun;12(6):e0177318.
84. Henke C, Spiesshoefer J, Kabitz H-J, Herkenrath S, Randerath W, Brix T, Görlich D, Young P, Boentert M. Characteristics of respiratory muscle involvement in myotonic dystrophy type 1. Neuromuscul Disord. 2020 Jan;30(1):17–27.
85. Kaminska M, Browman F, Trojan DA, Genge A, Benedetti A, Petrof BJ. Feasibility of Lung Volume Recruitment in Early Neuromuscular Weakness: A Comparison Between Amyotrophic Lateral Sclerosis, Myotonic Dystrophy, and Postpolio Syndrome. PM&R. 2015 Jul;7(7):677–84.
86. Leonardis L, Podnar S. Template-operated MUP analysis is not accurate in the diagnosis of myopathic or neuropathic changes in the diaphragm. Neurophysiol Clin. 2017 Dec;47(5–6):405–12.
87. Lucena Araújo T, Regiane Resqueti V, Bruno S, Guerra Azevedo I, Dourado Júnior ME, Fregonezi G. Respiratory muscle strength and quality of life in myotonic dystrophy patients. Rev Port Pneumol (English Ed. 2010 Nov;16(6):892–8.

88. Poussel M, Kaminsky P, Renaud P, Laroppe J, Pruna L, Chenuel B. Supine changes in lung function correlate with chronic respiratory failure in myotonic dystrophy patients. Respir Physiol Neurobiol. 2014 Mar;193:43–51.

89. Poussel M, Thil C, Kaminsky P, Mercy M, Gomez E, Chaouat A, Chabot F, Chenuel B. Lack of correlation between the ventilatory response to CO2 and lung function impairment in myotonic dystrophy patients: Evidence for a dysregulation at central level. Neuromuscul Disord. 2015 May;25(5):403–8.

90. Rossi S, Della Marca G, Ricci M, Perna A, Nicoletti TF, Brunetti V, Meleo E, Calvello M, Petrucci A, Antonini G, Bucci E, Licchelli L, Sancricca C, Massa R, Rastelli E, Botta A, Di Muzio A, Romano S, Garibaldi M, Silvestri G. Prevalence and predictor factors of respiratory impairment in a large cohort of patients with Myotonic Dystrophy type 1 (DM1): A retrospective, cross sectional study. J Neurol Sci [Internet]. 2019 Apr;399:118–24. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0022510X19300735

91. Seijger CGW, Drost G, Posma JM, van Engelen BGM, Heijdra YF. Overweight Is an Independent Risk Factor for Reduced Lung Volumes in Myotonic Dystrophy Type 1. Shi W, editor. PLoS One. 2016 Mar;11(3):e0152344.

92. Wenninger S, Stahl K, Wirner C, Einvag K, Thiele S, Walter MC, Schoser B. Utility of maximum inspiratory and expiratory pressures as a screening method for respiratory insufficiency in slowly progressive neuromuscular disorders. Neuromuscul Disord. 2020 Aug;30(8):640–8.

93. West SD, Lochmüller H, Hughes J, Atalaia A, Marini-Bettolo C, Baudouin S V., Anderson KN. Sleepiness and Sleep-related Breathing Disorders in Myotonic Dystrophy and Responses to Treatment: A Prospective Cohort Study. J Neuromuscul Dis. 2016 Nov;3(4):529–37.

94. Petitclerc É, Hébert LJ, Desrosiers J, Gagnon C. Lower limb muscle impairment in myotonic dystrophy type 1: The need for better guidelines. Muscle Nerve. 2015 Apr;51(4):473–8.

95. Whittaker RG, Ferenczi E, Hilton-Jones D. Myotonic dystrophy: practical issues relating to assessment of strength. J Neurol Neurosurg Psychiatry. 2006 Nov;77(11):1282–3.

96. Gagnon C, Heatwole C, Hébert LJ, Hogrel J-Y, Laberge L, Leone M, Meola G, Richer L, Sansone V, Kierkegaard M. Report of the third outcome measures in myotonic dystrophy type 1 (OMMYD-3) international workshop Paris, France, June 8, 2015. J Neuromuscul Dis [Internet]. 2018 Oct 23;5(4):523–37. Available from: https://www.medra.org/servlet/aliasResolver?alias=iospress&doi=10.3233/JND-180329

97. Marwick TH, Neubauer S, Petersen SE. Use of Cardiac Magnetic Resonance and Echocardiography in Population-Based Studies. Circ Cardiovasc Imaging. 2013 Jul;6(4):590–6.

98. Simpson R, Bromage D, Dancy L, McDiarmid A, Monaghan M, McDonagh T, Sado D. 6 Comparing echocardiography and cardiac magnetic resonance measures of ejection fraction: implications for HFMRF research. In: British Cardiovascular Imaging Meeting 2018. BMJ Publishing Group Ltd and British Cardiovascular Society; 2018. p. A3.1-A3.

99. Kaminska M, Noel F, Petrof BJ. Optimal method for assessment of respiratory muscle strength in neuromuscular disorders using sniff nasal inspiratory pressure (SNIP). Zissel G, editor. PLoS One. 2017 May;12(5):e0177723.

100. Bellemare F, Grassino A. Force reserve of the diaphragm in patients with chronic obstructive pulmonary disease. J Appl Physiol. 1983 Jul;55(1):8–15.

101. ATS/ERS Statement on Respiratory Muscle Testing. Am J Respir Crit Care Med. 2002 Aug;166(4):518–624.