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Magnetic resonance imaging patterns of muscle involvement in genetic muscle diseases: a systematic review

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Abstract

A growing body of the literature supports the use of magnetic resonance imaging as a potential biomarker for disease severity in the hereditary myopathies. We performed a systematic review of the medical literature to evaluate patterns of fat infiltration observed in magnetic resonance imaging studies of muscular dystrophy and congenital myopathy. Searches were performed using MEDLINE, EMBASE, and grey literature databases. Studies that described fat infiltration of muscles in patients with muscular dystrophy or congenital myopathy were selected for full-length review. Data on preferentially involved or spared muscles were extracted for analysis. A total of 2172 titles and abstracts were screened, and 70 publications met our criteria for inclusion in the systematic review. There were 23 distinct genetic disorders represented in this analysis. In most studies, preferential involvement and sparing of specific muscles were reported. We conclude that magnetic resonance imaging studies can be used to identify distinct patterns of muscle involvement in the hereditary myopathies. However, larger studies and standardized methods of reporting are needed to develop imaging as a diagnostic tool in these diseases.

Keywords

Magnetic resonance imaging; Muscular dystrophy; Congenital myopathy; Distal myopathy

Introduction

Since the introduction of clinical magnetic resonance imaging (MRI), investigators in the radiographic sciences have noted the ability of MRI to produce high-resolution anatomic images of skeletal muscle. Unlike prior imaging modalities, MRI provides excellent contrast between various soft tissue structures, allowing for the examination of individual muscles in sharp contrast to adjacent fat [1]. In recent years, MRI of muscle has gained wider clinical use in the inflammatory myopathies, where the introduction of new immunosuppressive

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Compliance with ethical standards

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Ethical standards The manuscript does not contain clinical studies or patient data.

agents has created a need for tools that can accurately diagnose and monitor response to treatment. The ability of MRI to distinguish between acute inflammation and chronic fatty replacement in muscle also provides important prognostic information [2].

In the muscular dystrophies and other hereditary myopathies, the clinical use of MRI as a diagnostic modality has not entered into the standard of care for multiple reasons. First, genetic testing has become increasingly available and affordable, and it offers highly specific diagnostic information that cannot be achieved with muscle imaging. The relative absence of large studies in this diverse patient population also makes the interpretation of MRI scans difficult. There are also relatively few medical treatments for hereditary muscle disorders compared to the inflammatory myopathies and, subsequently, fewer ways in which MRI can influence medical decision-making.

Despite these known limitations, there is growing interest in using imaging (and MRI in particular) in research studies of hereditary muscle disease [3, 4]. Early trials in this disease population have highlighted the limitations of existing outcome measures for muscular dystrophy [5]. An objective, non-invasive measure that can be repeated many times could significantly improve the quality of trials in these diseases.

The purpose of this review is to examine the methods with which researchers have used MRI to study genetic myopathies and identify patterns of muscle involvement reported in the scientific literature. A systematic examination of the literature also provides an opportunity to identify obstacles that need to be addressed in the field of muscle imaging.

Methods

Literature searches

A search of the literature was performed in accordance with methods described by the Cochrane Handbook for Systematic Review of Interventions [6]. Controlled vocabulary and keyword searches were performed using the MEDLINE and EMBASE databases. Search terms were selected based on two concepts: genetic muscle disease (“muscular dystrophy” or “congenital myopathy”) and magnetic resonance imaging (“magnetic resonance imaging” or “MRI” or “magnetic resonance spectroscopy” or “MRS”). We did not restrict our searches with regard to publication date, allowing the search to include all articles published from the time of database inception to the date of the literature search (10/05/2016). We further evaluated reference lists from included articles and completed forward citation searching using the Web of Science database to identify additional citations. Abbreviated search strategies were used to search for relevant information in the Cochrane Library, OpenSIGLE (System for Information on Grey Literature in Europe), and the New York Academy of Medicine Grey Literature Report and Database.

Study selection

All titles and abstracts were reviewed, and studies were excluded based on the following criteria: (1) the study was not performed in humans; (2) the study did not analyze a majority of the skeletal muscles in at least one segment of one limb (such as the lower leg or thigh); (3) the study did not describe a genetically distinct muscular dystrophy, congenital

myopathy, or distal myopathy; (4) the study did not isolate results of MRI studies from those of other imaging modalities (such as computed tomography); (5) the study described only a single kindred; (6) the study described fewer than four subjects; (7) the methods did not report or cite a system for scoring individual muscles based on fat infiltration; (8) the manuscript was a review or editorial publication that did not report primary research data; (9) study was not published in English; and (10) full-text versions of the article were not obtainable. The full-text versions of studies that met these criteria based on titles and abstracts were downloaded and reviewed. Studies that did not meet these inclusion criteria after full-text review were subsequently excluded.

Data extraction and synthesis

The studies that were selected for analysis based on full-text review underwent data extraction. The following information about each study was collected: first author, year of publication, study type, phenotype of study sample, genotype of study sample, number of MRI scans analyzed, regions imaged, and scoring system used for assessment of fat infiltration. In studies where multiple genetic diseases were described, each genetically distinct population was reported as a separate entry in the table. Data on muscles that were preferentially affected and spared in each study population were also collected. Muscles were considered preferentially affected if they were defined by the authors as the earliest, most severely, or most frequently infiltrated by fat across the study sample. Muscles were counted as preferentially spared if they were defined by the authors as relatively spared when compared to other muscles within an individual subject or were less frequently or severely involved across the study sample. The extracted data were stored in tabular form, with “?” signifying preferential involvement, “-” signifying sparing, “??” signifying the most preferentially involved muscle, and “-” signifying the most preferentially spared muscle. In instances where an entire muscle group was listed instead of an individual muscle, all muscles within that group were coded equally. However, if regions comprised of more than one muscle group were listed (for instance, “all pelvic muscles”) and the muscles within those regions were not explicitly defined, these groups were not coded. For studies where a list of muscles ranked in order of fat infiltration was provided without further description of preferential involvement, only the highest and lowest ranked muscles were coded.

The degree of heterogeneity between studies was assessed through subgroup analyses in which studies were stratified by disease phenotype, genotype, study type, scoring technique, sample size, and regions imaged.

Results

Study selection

The search strategy identified 2172 unique citations (Fig. 1) [7]. Screening of titles and abstracts resulted in the exclusion of 1870 citations. A full-text review of the remaining 302 articles yielded 70 that were included in the final analysis. These studies were published between 1993 and 2016. Because some of these texts reported more than one genetic disease, there were 87 discrete disease populations (“cohorts”) included in the analysis. These cohorts included a total of 1918 MRI scans [8–77].

Characteristics of included studies

The included studies reported data from 23 different genetic myopathies (Table 1). The number of studies for each disease varied widely (range 1–23), with the dystrophinopathies and facioscapulohumeral muscular dystrophy (FSHD) accounting for the largest numbers of studies (23 and 14 studies, respectively). The dystrophinopathies and FSHD each account for approximately one-third of the scans described, with the remaining 21 genetic diseases comprising the remaining third. The number of MRI scans analyzed in each study also varied widely (range 4–269). However, most cohorts were small (median 13, mean 22 scans), and only three included more than 100 scans.

Most of the studies selected for review used a cross-sectional study design, meaning that enrolled subjects were scanned once. Only five studies included longitudinal follow-up imaging. Thirteen of the 70 articles reported the inclusion of healthy controls. Fourteen of the 70 articles reported the inclusion of diseased controls or multiple types of hereditary myopathy.

The majority of studies used a semi-quantitative scoring system with 4, 5, or 6 grades to rank individual muscles (Table 2). Higher numerical scores were used to signify more extensive fat infiltration. The specific muscle characteristics and cutoffs for each grade varied between studies; 25 cohorts were scored using a cutoff point of 50% fat infiltration (described by Jungbluth et al.) to denote changes in severity grade, and 34 cohorts were scored using cutoffs of 30 and 60% fat infiltration (described by Mercuri et al.) [64, 78]. Eight cohorts did not use specific cutoff percentages (the Lamminen scale) [79]. Only 20 of the 87 disease cohorts (13 dystrophinopathy, 4 FSHD, 2 myotonic dystrophy, and 1 MYH7-myopathy) were analyzed using alternative scoring systems. It is notable that of these 20, 15 were reported in articles published within the past five years and utilized fully quantitative methods of determining the amount of fat infiltration in muscle.

The majority of studies imaged the lower extremities, with 51 of the 87 cohorts exclusively imaging the lower extremities (lower leg, thigh, or pelvis). Thirty-two studies imaged the lower extremities and at least one other region of the body (trunk, shoulder, arm, or head/neck), and only four of the 87 cohorts reported imaging of the upper extremities only. Seventeen of the cohorts (described in 11 separate manuscripts) reported using whole-body MRI, or scanning of contiguous anatomic regions that included the arms, trunk, and legs. In 73 of the 87 cohorts (including all of the studies that used a semi-quantitative scoring system), analysis of fat infiltration was performed on T1-weighted images. Nine studies used Dixon sequences to calculate muscle fat fractions, and two used T2-based sequences to calculate fat fractions or ratios. Three studies used more than one type of sequence to analyze fat infiltration (T1-weighted imaging plus either proton density or Dixon imaging).

The dystrophinopathies

For the purposes of pattern analysis, dystrophinopathies were divided into three phenotypic subcategories (Duchenne, Becker, and carrier). While sharing a common genetic origin, the clinical characteristics and prognosis of these phenotypes vary widely. The Becker phenotype is milder than the Duchenne phenotype, while the majority of female carriers are

asymptomatic. Despite these clinical disparities, the reported patterns of muscle involvement across all dystrophinopathies were similar. More than half of the studies that included imaging of the thigh reported preferential involvement of the gluteus maximus, gluteus medius, and adductor magnus with sparing of the gracilis and sartorius (Table 3). The dystrophinopathy studies included the widest variety of scoring techniques for fat infiltration, with only about half using a semi-quantitative scoring system. The remaining studies used fully quantitative techniques to characterize fat replacement. Nine of these studies quantified the muscle fat fraction, or the percentage of muscle replaced by fat.

Facioscapulohumeral muscular dystrophy

Fourteen studies reported MRI findings in individuals with FSHD (Table 4). This group of studies showed the greatest anatomic diversity, with almost half of the studies imaging regions other than the legs. MRI of the arms is technically more challenging than imaging of the legs, and the number of studies that included upper extremity imaging likely reflects the high prevalence of upper extremity involvement in FSHD. A consistent finding among the FSHD studies was the preferential involvement of the semimembranosus, which was reported to be the most severely involved muscle in 9 of the 11 studies that scanned the thigh. The medial gastrocnemius and tibialis anterior muscles were the most preferentially affected in the lower leg, while the tibialis posterior and peroneus were frequently spared. The hip flexors (iliopsoas and iliacus) were preferentially spared in multiple studies. However, in contrast to the dystrophinopathies and limb-girdle muscular dystrophies, the gracilis and sartorius were never reported to be preferentially spared. This may seem incongruous with prior observations of scans in which the gracilis and sartorius are spared relative to other muscles of the medial thigh (Supplemental Fig. 1). One possible explanation is that only a subset of patients with FSHD exhibits sparing of the gracilis and sartorius, and these muscles are not spared across the entire disease population.

Observations across all studies

Most genes had too few studies or were too heterogeneous to discern specific patterns of involvement (Tables 5, 6, 7). However, evaluation of imaging patterns across all 87 cohorts yielded several notable observations. Several muscles in the thigh (long head biceps femoris, semimembranosus, and adductor magnus) and lower leg (medial gastrocnemius and soleus) were the most likely to be reported to be preferentially involved across all studies. The gracilis, sartorius, and tibialis posterior were most frequently reported as spared across all studies. The rectus femoris, adductor longus, peroneus longus, and tibialis anterior were found to have a mix of preferential involvement and sparing in different diseases. In some cases, the preferential involvement or sparing was disease-specific. For instance, in studies describing FSHD, the tibialis anterior was reported to be preferentially involved, while the peroneus longus was found to be preferentially spared. In the dystrophinopathies, the reverse was true, with multiple studies reporting sparing of the tibialis anterior and involvement of the peroneus longus.

We also observed that the diseases with preferential involvement of the sartorius were either congenital myopathies or distal myopathies, while in the dystrophinopathies and limb-girdle muscular dystrophies, the sartorius was among the most frequently spared. Similarly, the

adductor longus was much more frequently spared in the congenital myopathies and congenital muscular dystrophies compared to the dystrophinopathies or limb-girdle muscular dystrophies. In most other diseases and muscles, however, there were too few studies or scans to define a consistent pattern of involvement.

Some radiographic features that are specific to a particular disease were noted in this analysis. All the studies describing collagen VI disorders reported that the outer rim of the vastus lateralis was replaced by fat before the center of the muscle. The majority of these studies also reported a strip or notch of fat replacement in the center of the rectus femoris (Table 6). Multiple studies describing type 1 myotonic dystrophy reported a crescent-shaped region of involvement in the quadriceps resulting from preferential involvement of the vastus intermedius and vastus medialis compared to the vastus lateralis [50, 74, 80]. In the majority of studies, however, no similarly distinctive disease-defining features were reported.

Discussion

This review raises several important points about the role of MRI in the study of muscle disease. The identification of patterns of muscle involvement and sparing in different types of muscular dystrophy suggests that skeletal muscle imaging could be used in a diagnostic capacity. While MRI does not offer the specificity of gene testing and there is substantial overlap in the imaging findings in a number of myopathies, there are clinical scenarios in which MRI could be diagnostically useful. For instance, MRI may be helpful in distinguishing hereditary from acquired myopathies, which could impact medical management considerably. Muscle MRI could also have a role in determining the pathogenicity of variants of unknown significance identified through genetic testing.

The number of recent studies that used quantitative methods to evaluate fat infiltration may indicate a growing interest in using muscle MRI for research in hereditary muscle disease. Several characteristics of muscle MRI make it a promising a research tool for clinical trials and longitudinal studies. MRI scans are repeatable, non-invasive, and non-irradiating; furthermore, scanned images can be easily de-identified and stored for analysis by blinded reviewers. Compared to strength and function tests, MRI measurements may also be less vulnerable to confounding by the level of cooperation and effort on the part of the study subject. Although only one of the studies selected for this review was an interventional study [43], several clinical trials of novel drugs in muscular dystrophy have reported using MRI as a secondary outcome measure, and at least one trial has reported using MRI as a primary outcome measure (clinicaltrials.gov NCT02515669, NCT02310763, and NCT02927080) [81, 82].

The variability between studies of the same genetic disorder bears closer inspection. While the differences in reported patterns of muscle involvement are likely due in part to differences in scoring and reporting techniques, it is also possible that contradictory findings could reflect the presence of distinct subgroups within a disease population. The increasing use of genetic testing has shown that in some genetic diseases, phenotypic variability is wider than was previously suspected. A number of genes, such as collagen VI, are associated with more than one clinical phenotype, and genotyping studies in FSHD have

shown that individuals who carry a disease-causing mutation can be asymptomatic or minimally affected [83, 84]. It is also worth noting that not all studies used genetic testing as a requirement for inclusion (the dystrophinopathies, for instance, may have been diagnosed through muscle biopsy), and there could be unrecognized genotypic variability within a study sample.

The results of this analysis also show that the field of MRI for muscular dystrophy is dominated by the dystrophinopathies and FSHD. This likely reflects not only the relative frequency of these disorders, but also the activity of subspecialty research centers, patient registries, and advocacy groups. The relative paucity of scans in other diseases compels caution in drawing conclusions about patterns of muscle involvement in these disorders, as small studies in selected populations may be subject to selection bias. Such bias could be further amplified by overlap in the study samples reported in multiple manuscripts from the same investigator group. In the extremely rare muscular dystrophies, the collection of sufficient numbers of scans to adequately characterize the disease population may only be achievable through collaborations between multiple centers.

There are some limitations to this qualitative review. First, we did not discriminate between different types of preferential involvement or sparing. Preferential involvement could mean the most frequently affected, the earliest affected, or the most severely affected muscles. Likewise, preferential sparing could mean that a muscle is universally spared across the cohort or relatively spared compared to other muscles in the same region. We relied on the authors to report preferentially involved or spared muscles in cases where the primary data were not provided in the manuscript text or figures, and the criteria for identifying these muscles was infrequently reported. For future observational studies and clinical trials, it will be essential to develop a uniform system of classifying and reporting imaging findings.

Our eligibility criteria for inclusion in the qualitative review were prospectively established with the purpose of minimizing risk of bias in the included studies. However, these criteria resulted in the exclusion of several important imaging studies that utilized computed tomography (CT) or a combination of CT and MRI [78, 85, 86]. While CT can identify fat infiltration in muscle, it has not been established that scoring results from MRI are exchangeable with those from CT. The eligibility criteria also excluded metabolic myopathies, mitochondrial myopathies, and non-dystrophic myotonias (the muscle ion channel disorders). While imaging studies have been performed in these disorders, fat replacement of muscle is not a universally reported feature in these diseases, and appropriate comparisons with regard to preferential muscle involvement could not be made [87–90].

Another potential limitation of this review is that we were unable to stratify imaging findings based on important confounders in muscular dystrophy, such as gender, age of onset (or duration of disease symptoms), age, distribution of weakness, or mutation type. At least one of the included studies reported that there were differences in the patterns of muscle involvement between males and females [51]. However, the reporting of these potential confounders was too inconsistent between manuscripts to allow substantive analysis of their impact. Our analysis also only included data on fat infiltration and did not include other features of muscle disease, such as edema-like changes, muscle hypertrophy, or atrophy.

These features represent additional aspects of disease pathology that merit further characterization.

The results of this review underline several factors that should be considered in studies using MRI in muscle disease. First is the need for greater standardization across all stages of imaging, from the selection of participants and imaging sequences to the scoring and reporting of collected images. Standardized methodologies will facilitate the extraction and synthesis of findings across multiple investigator groups [91]. Second, the radiographic phenotype can differ considerably from clinical observations. For instance, several studies reported that the medial gastrocnemius muscle is as frequently or more frequently affected than the tibialis anterior in FSHD. However, foot drop is more frequently observed than calf weakness in this disease population. This may be due to the fact that there are multiple muscles involved in ankle plantarflexion, all of which are larger than the tibialis anterior. Extensive replacement of a single muscle may not be clinically apparent if other members of the same muscle group remain intact. It is also important to consider that many of the reviewed studies are fairly small case series in which a well-defined clinical population was selected for imaging. In these cases, we may expect imaging findings to be fairly homogeneous. As imaging studies expand to include more atypical cases from a greater number of centers, we would expect the radiographic phenotypes of these disorders to be more heterogeneous as well.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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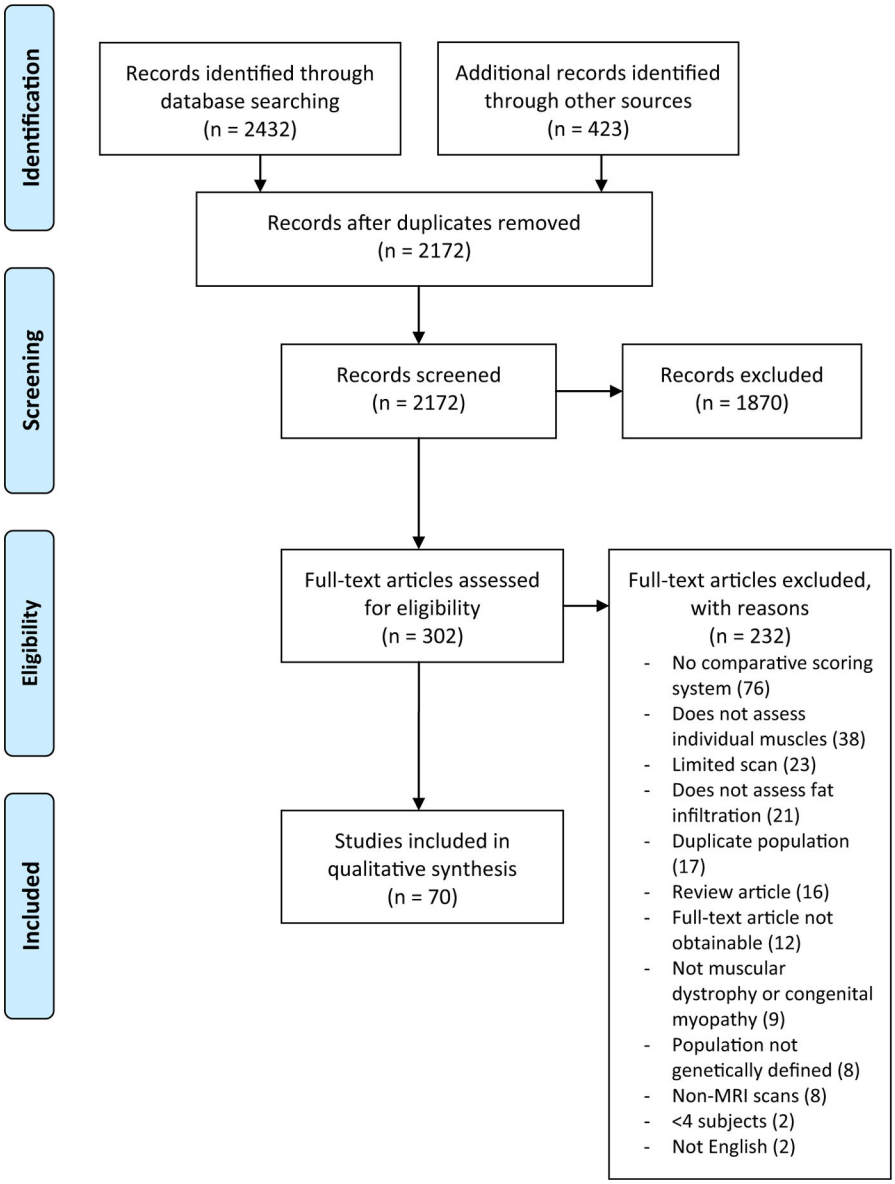


Fig. 1.
PRISMA (preferred reporting items for systematic reviews and meta-analyses)

Table 1

Numbers of studies and scans for each genetic disorder included in systematic review

Gene	Number of studies	Total number of scans	Percentage of studies	Percentage of scans
ACTA1	1	4	1.1	0.2
COL6	5	58	5.7	3.0
DES	1	4	1.1	0.2
DMPK	7	99	8.0	5.2
CNBP	3	23	3.4	1.2
DMD	23	689	26.4	35.9
Duchenne	16	554	18.4	28.9
Becker	6	123	6.9	6.4
Carrier	1	12	1.1	0.6
FSHD	14	617	16.1	32.2
CAPN	3	22	3.4	1.1
DYSF	6	143	6.9	7.5
FKRP	3	51	3.4	2.7
ANO5	2	30	2.3	1.6
LMNA	4	38	4.6	2.0
MATR3	1	16	1.1	0.8
MYOT	2	13	2.3	0.7
NEB	1	6	1.1	0.3
PABN	2	18	2.3	0.9
RYR1	2	15	2.3	0.8
SEPN1	2	13	2.3	0.7
TTN	1	22	1.1	1.1
TPM2	2	12	2.3	0.6
TIA1	1	11	1.1	0.6
MYH7	1	14	1.1	0.7
Total	87	1918	100.0	100.0

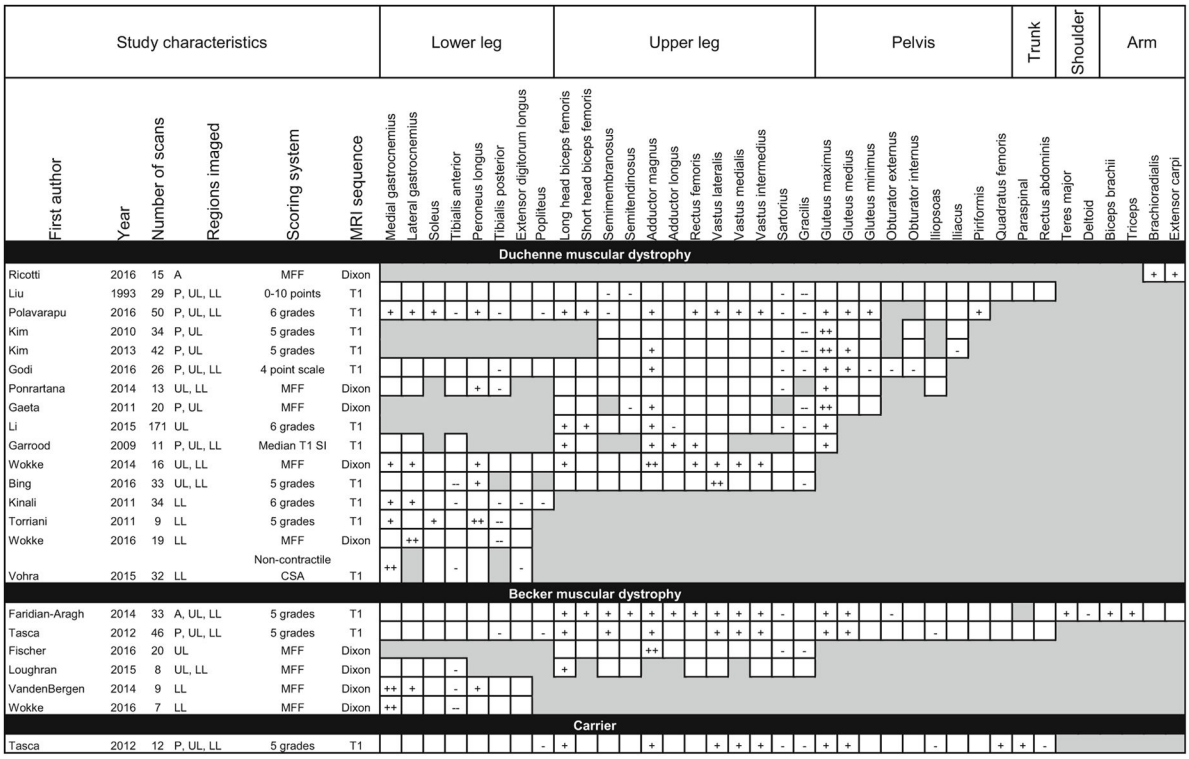
Table 2

Majority of studies selected for review used a variant of one of the following three scoring systems

Score	Lamminen [79]	Mercuri et al. [59, 78]	Jungbluth et al. [62, 64]
0		Normal	Normal
1	Normal muscle signal intensity	Early moth-eaten appearance, with scattered small areas of increased density on T1 MRI	Mild with only traces of increased signal intensity
2	Slightly hyperintense, patchy intramuscular signal changes	A: Late moth-eaten appearance, with numerous discrete areas of increased density with beginning confluence, comprising less than 30% of the volume of the individual muscle B: Late moth-eaten appearance, with numerous discrete areas of increased density with beginning confluence, comprising 30–60% of the volume of the individual muscle	Moderate with increased signal in less than 50% of affected muscle
3	Markedly hyperintense, patchy but widespread intramuscular changes	Washed-out appearance, fuzzy appearance due to confluent areas of increased density with muscle still present at the periphery	Severe with increased signal intensity in more than 50% of affected muscle
4	Total, homogeneous hyperintense signal change in whole muscle, equaling the signal intensity of adjacent subcutaneous or paramuscular fat	End-stage appearance, muscle replaced by increased density connective tissue and fat with only rim of fascia and neurovascular structures distinguishable	Entire muscle replaced by abnormal signal

Table 3

Patterns of muscle involvement and sparing in MRI studies describing populations with mutations in dystrophin

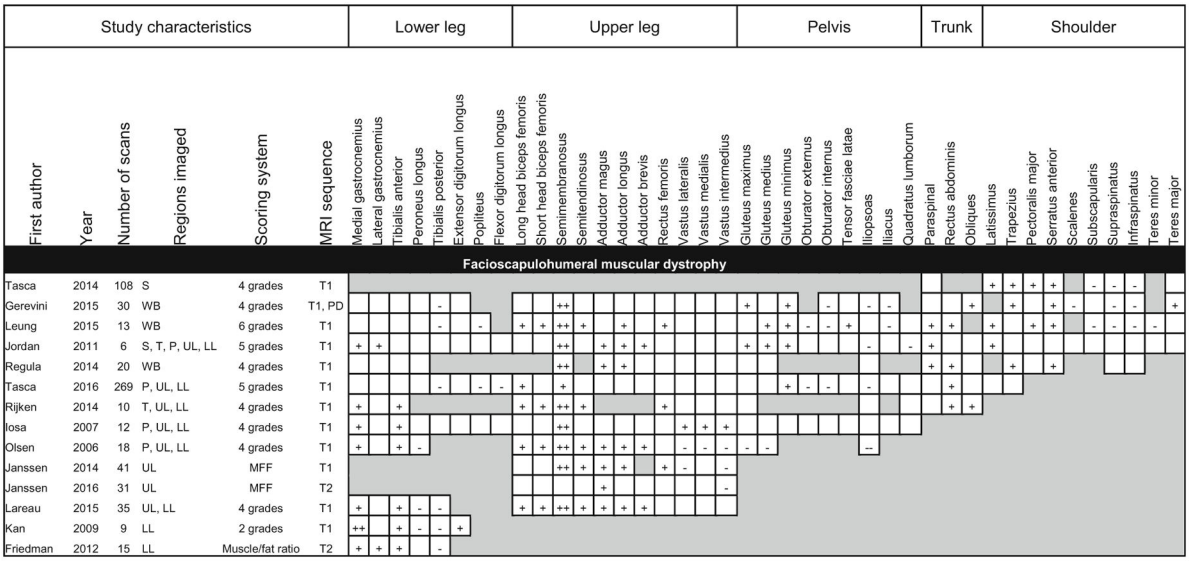


Shaded boxes represent muscles that were not scanned or analyzed

MFF muscle fat fraction, *CSA* cross-sectional area, *A* arm, *P* pelvis, *UL* upper leg, *LL* lower leg

Table 4

Patterns of muscle involvement and sparing in MRI studies describing facioscapulohumeral muscular dystrophy

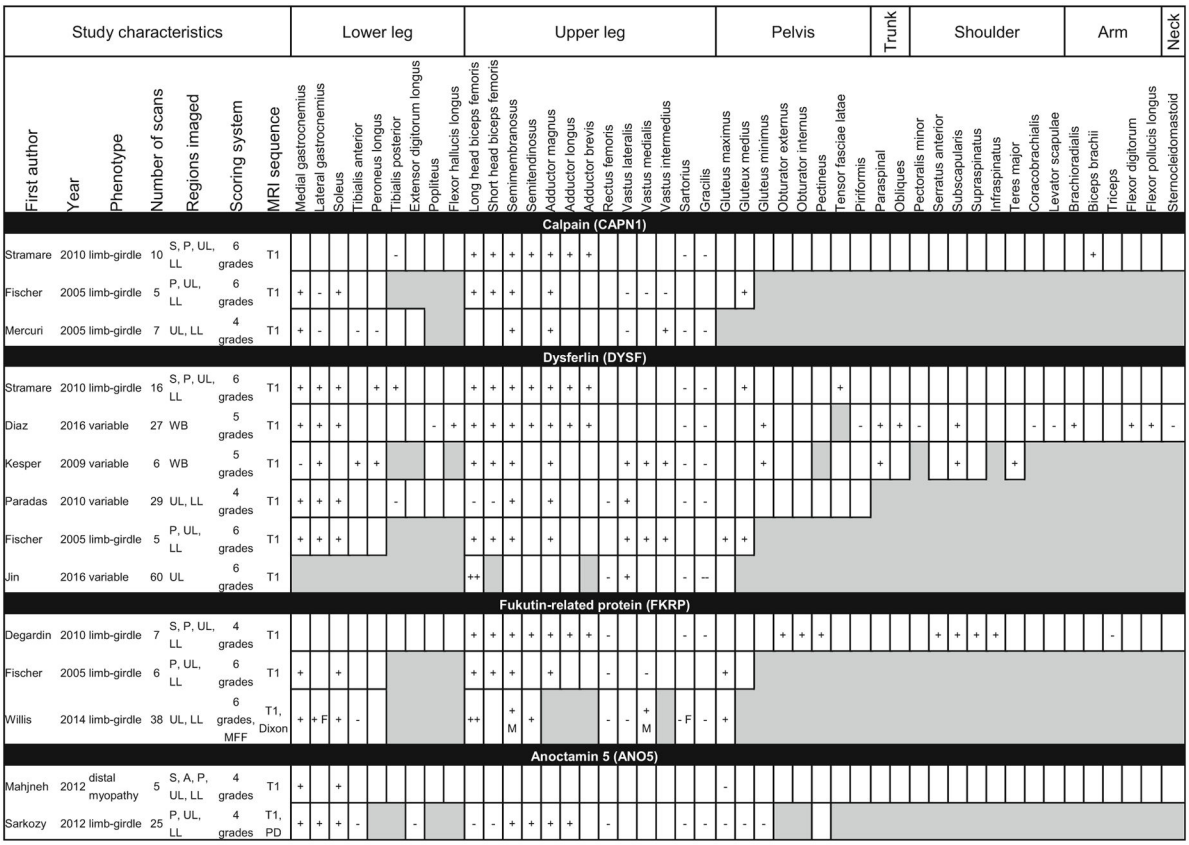


Shaded boxes represent muscles that were not scanned or analyzed

MFF muscle fat fraction, *PD* proton density, *S* shoulder, *T* trunk, *P* pelvis, *UL* upper leg, *LL* lower leg, *WB* whole-body

Table 5

Patterns of muscle involvement and sparing in MRI studies describing limb-girdle muscular dystrophy

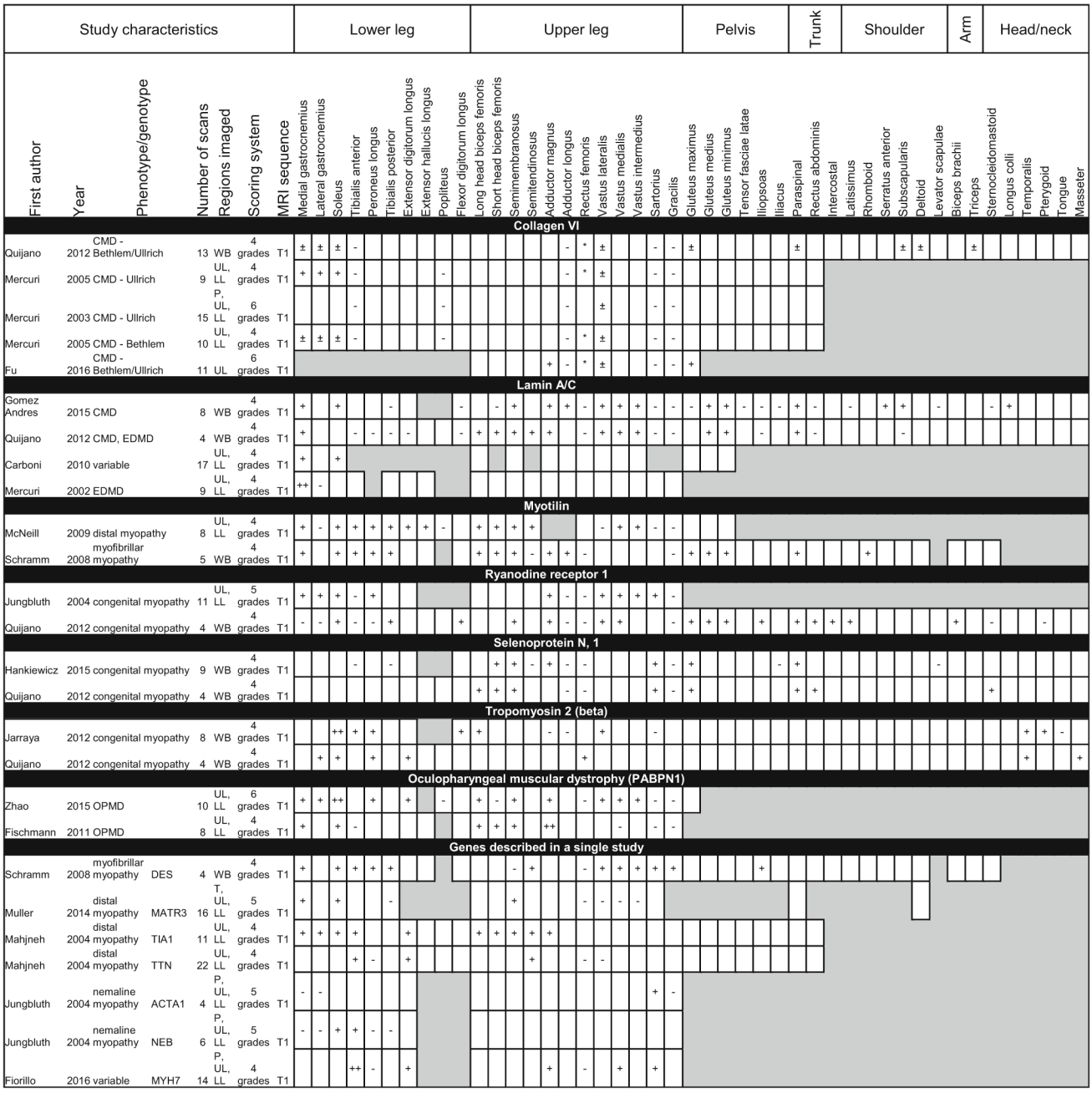


Shaded boxes represent muscles that were not scanned or analyzed. M and F denote findings seen only in males or females, respectively

MFF muscle fat fraction, *A* arm, *S* shoulder, *P* pelvis, *UL* upper leg, *LL* lower leg, *WB* whole-body

Table 6

Patterns of muscle involvement and sparing in MRI studies describing congenital myopathy, congenital muscular dystrophy (CMD), Emery–Dreifuss muscular dystrophy (EDMD), distal myopathy, and oculopharyngeal muscular dystrophy (OPMD)

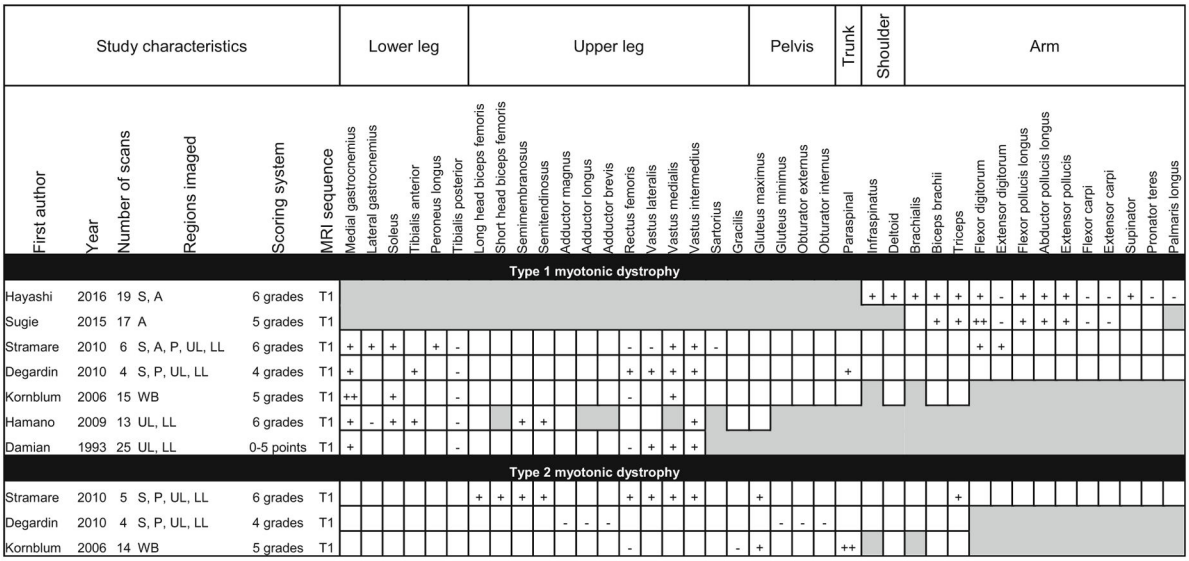


Shaded boxes represent muscles that were not scanned or analyzed. A * denotes fat replacement in the center of the muscle. A ± denotes fat replacement at the muscle periphery

T trunk, *P* pelvis, *UL* upper leg, *LL* lower leg, *WB* whole-body

Table 7

Patterns of muscle involvement and sparing in MRI studies describing myotonic dystrophy



Study characteristics							Lower leg						Upper leg																				Pelvis					Trunk	Shoulder		Arm																
First author	Year	Number of scans	Regions imaged	Scoring system	MRI sequence	Medial gastrocnemius	Lateral gastrocnemius	Soleus	Tibialis anterior	Peroneus longus	Tibialis posterior	Long head biceps femoris	Short head biceps femoris	Semimembranosus	Semitendinosus	Adductor magnus	Adductor longus	Adductor brevis	Rectus femoris	Vastus lateralis	Vastus medialis	Vastus intermedius	Sartorius	Gracilis	Gluteus maximus	Gluteus minimus	Obturator externus	Obturator internus	Paraspinal	Infraspinatus	Deltoid	Brachialis	Biceps brachii	Triceps	Flexor digitorum	Extensor digitorum	Flexor pollucis longus	Abductor pollucis longus	Extensor pollucis	Flexor carpi	Extensor carpi	Supinator	Pronator teres	Palmaris longus
Type 1 myotonic dystrophy																																																					
Hayashi	2016	19	S, A	6 grades	T1																								+	+	+	+	+	+	-	+	+	+	-	-	+	-	-
Sugie	2015	17	A	5 grades	T1																												+	+	++	-	+	+	+	-	-			
Stramare	2010	6	S, A, P, UL, LL	6 grades	T1	+	+	+		+	-								-	-	+	+	-												+	+										
Degardin	2010	4	S, P, UL, LL	4 grades	T1	+			+		-								+	+	+	+							+																	
Kornblum	2006	15	WB	5 grades	T1	++		+			-								-		+																									
Hamano	2009	13	UL, LL	6 grades	T1	+	-	+	+		-			+	+							+																							
Damian	1993	25	UL, LL	0-5 points	T1	+					-								-	+	+	+																							
Type 2 myotonic dystrophy																																																				
Stramare	2010	5	S, P, UL, LL	6 grades	T1							+	+	+	+				+	+	+	+			+									+											
Degardin	2010	4	S, P, UL, LL	4 grades	T1											-	-	-								-	-	-																	
Kornblum	2006	14	WB	5 grades	T1														-				-	+				++																	

Shaded boxes represent muscles that were not scanned or analyzed

A arm, *S* shoulder, *P* pelvis, *UL* upper leg, *LL* lower leg, *WB* whole-body